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# MERCURIAL PESTICIDES, MAN, AND THE ENVIRONMENT

Environmental Protection Agency
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1971

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# MERCURIAL PESTICIDES, MAN, AND THE ENVIRONMENT

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ENVIRONMENTAL PROTECTION AGENCY
1971

Prepared by the Special Pesticide Review Group of the Office of Pesticides Programs, Environmental Protection Agency.

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## ABOUT THIS REPORT

This staff report represents a scientific and technical assessment of mercurial products registered with the U.S. Environmental Protection Agency for pest control purposes. This information was developed to assist the Agency in evaluating the past, present, and future impact of these pesticides on man and his environment prior to determining whether their continued use is in the public interest.

In making this determination, the Agency also will consider data supplied by other scientific sources, both governmental and private, as well as pertinent economic and social factors. Therefore, any conclusions and recommendations for action contained in this preliminary report should not be construed as the position of the EPA or necessarily indicative of the course of action it might finally take with regard to mercurial pesticides.

# MERCURIAL PESTICIDES, MAN, AND THE ENVIRONMENT

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## INTRODUCTION

The realization of the toxicity of mercury dates back as far as recorded history. Hippocrates (460-377 B.C.). Pliney the Elder (23-79 A.D.). Galen (131-200 A.D.). Avicenna (980-1037 A.D.). and Paracelsus (1493-1541 A.D.) have all written on the toxic effects of mercury (Battigelli. 1960; Goldwater. 1957). The first mention of mercury as an industrial hazard appeared in the middle of the 19th century in connection with hatters employing mercury nitrate in the felting process. In spite of the early realization of the hazard involved with this use of mercury. it continued until recent times. In 1941. the U.S. Public Health Service published the results of a field study showing that more than 10% of the workers examined were suffering from chronic mercury poisoning (Neal. 1941). The expression "mad as a hatter" is believed to have originated as a result of one of the toxic manifestations of mercury poisoning. The hazard in this industry as well as in many others. e.g.. mining. manufacture of thermometers and barometers. testing departments. and laboratories has been either eliminated or greatly reduced.

Although progress has been made in industrial safety. "epidemic" outbreaks of chronic mercury poisonings still occur. This is due. in part. to the extensive increase in the industrial and agricultural uses of mercury in recent decades. In 1958. Benning described mercury intoxication in more than 60 workers in an Ohio plant employed in the manufacture of carbon brushes. In another episode. inhalation of mercury vapors from a mercury-containing paint was implicated in an outbreak of neuromyasthenia in a Kentucky electronics plant (Miller *et al.*. 1967).

Reports of poisonings resulting from the use of alkylmercury seed disinfectants soon followed their introduction. In 1940 Hunter. *et al* described in detail four cases of alkylmercury poisonings resulting from industrial exposure. Ahlmark (1948) described five cases of poisoning (two fatal) of workmen involved in manufacture and handling of methylmercury compounds. In 1949. Lundgren and Swensson reported eight cases of occupational poisoning by alkylmercury compounds. Between 1956 and 1960. there were over three hundred patients suffering from mercuric poisoning admitted to hospitals in Mosul and Baghdad. Iraq. They had consumed wheat treated with ethylmercury toluene sulfonanilide (Jalili and Abbasi. 1961). Similar episodes occurred in Pakistan (Haq. 1963) and Guatemala. (Ordones. *et al.* 1966). Numerous other cases of poisoning with alkylmercury compounds have been reported in the literature and by the press. The most recent and the most publicized in this country occurred in Alamogordo. N. M.. in 1969. when three members of one family were poisoned from eating pork from hogs which had been fed grain treated with an alkylmercury pesticide.

During the past 20 years. there have been two occurrences of human mercury poisoning in Japan resulting from the eating of contaminated fish. The first incident occurred in Minamata in 1953. The outbreak reached almost epidemic proportions. The source of contamination was traced to a vinylchloride and acetaldehyde plant which discharged large quantities of methylmercury into Minimata Bay. From 1953 to 1970. 121 persons were reported poisoned after having eaten fish and shellfish caught in Minimata Bay.

There were 46 deaths recorded. It was some time before Japanese medical authorities recognized and documented the similar clinical disorder of a large number of people in the Minamata area. A second incident occurred in the riverside villages of the Agano River in Niigata prefecture where 47 cases and six deaths were observed through 1970.

This syndrome, which has become to be known as the "Minamata disease" is characterized by widespread involvement of the central nervous system with granular cell degeneration of the cerebellum, and lesser involvement of the basal ganglia, hypothalamus, midbrain, and cerebral cortex. The relative ease with which methylmercury passes the "blood-brain barrier" in humans accounts for the severe neurologic manifestations.

The staff of the Kumamoto University, in a series of carefully planned investigations, first identified the causative factor of Minamata disease as heavy consumption of fish contaminated with an organic form of mercury, later identified as methylmercury. Similar findings were made by the staff of the University of Niigata in the Niigata City and Agano River outbreaks (Nelson, *et al.* 1971).

The first warning of the mercury problem in Sweden came in the early 1950's when the populations of the yellow bunting dropped catastrophically. Deaths, reproductive failures and population declines of both seed-eating and raptorial birds were soon noted (Otterlind, *et al.* 1964). Toxicity from mercury used in seed dressings to prevent cereal diseases was suspected. Investigations proved this assumption to be correct. It was soon discovered that mercury pollution was serious in Swedish lakes, and that leakage from pulp mills and chlor-alkali factories was responsible.

Late in 1965, Westöö determined that the mercury she found in eggs, fish, and some other meats was methylmercury. Westöö observed that both fish and mammals could convert small amounts of inorganic mercury to methylmercury in their livers. It was shown that Swedish eggs had four times the mercury content of eggs from the rest of continental Europe. Johnels published an opinion that inorganic mercury could be converted to methylmercury by microorganisms in anaerobic ecosystems such as mud on lake bottoms. In 1965, it was shown that the mercury in samples of eggs, meat and fish from Sweden was 80 to 100% methylmercury. Subsequently, mercury has been shown to be methylated by aquarium and natural sediments (Jensen and Jernelov, 1969).

Because of mercury contamination, the marketing of fish from certain lakes and rivers has been banned in Sweden. This decision is based on a temporary limit of 1 mg Hg/kg of body weight with a recommendation not to eat fish from fresh waters more than once a week. Recent investigations in Denmark, Finland and Norway have demonstrated similar elevated mercury concentrations in fish from coastal waters.

The National Poisons and Pesticides Board of Sweden revoked the licenses for alkylmercury compounds in Agriculture on February 1, 1966. In the year following this ban, the mercury content of Swedish eggs fell almost to the level of the rest of continental Europe or one-third of the level reported in 1966.

In 1969, following warnings of significant mercury pollution in the central provinces, studies were initiated by the Canadian Wildlife Services to define the situation. Following these studies, several commercial catches of fish (walleye, northern pike, bass and jackfish) taken from Lake Winnipeg, Cedar Lake, Saskatchewan River, and Red River in Manitoba Province were seized by the Canadian Federal Department of Fisheries and Forestries, because they contained mercury residues ranging from 5 to 10 ppm (Seagran, 1970). The Canadian Government then publicly embargoed all commercial fish taken from Lake Saint Clair effective March 23, 1970.

In the United States, results of analytical studies on fish and wildlife showed mercury levels up to 117 ppm in eagles from Minnesota and up to 4.4 ppm in fish collected from the North Fork of the Holston River. As a result of this information, restrictions on sport and commercial fishing have been placed on waters within at least 18 states as of September 1970 (Celeste and Shane, 1970).

In the fall of 1970, the Food and Drug Administration found that canned tuna sold in the United States contained up to 1.2 ppm mercury (average 0.37 ppm) and that frozen swordfish ranged from 0.18 to 2.4 ppm (average 0.93 ppm). The Food and Drug Administration set an interim guideline of 0.5 ppm mercury in fish.

A 21 member *ad hoc* committee of experts reviewed the Food and Drug Administration's data on mercury contamination of swordfish and were unable to suggest any basis on which swordfish consumption might be continued without possible health hazard. Accordingly, the FDA issued the statement in May 1971 that the "public stop eating this fish until and unless the situation can be remedied."

On May 20, 1971, at a Senate subcommittee hearing on chemical pollution, the first case of mercury poisoning in the United States from eating fish was reported. Dr. Roger C. Herdman, New York State Deputy Health Commissioner, reported the case of a housewife, age 44. He stated that she became "rigidly committed" to a weight loss program. She started eating 10 oz of swordfish a day, plus some shrimp, for 10 months "without interruption." She lost 45 lb but began suffering lethargy, visual complaints and tremor. Still, two or three times a year until last November, she again ate swordfish for 3 to 6 weeks. In May 1966, she began having serious trouble speaking, walking, and understanding along with loss of memory and dizziness. Doctors told her it was probably psychosomatic, and she saw a psychiatrist once a week for 2 1/2 years. Only recently did a hair sample reveal a high mercury concentration (Washington Post, May 21, 1971).

## FOREWORD

*Charge* — In a statement issued on March 18, 1971, the Administrator of the Environmental Protection Agency said that "Active internal review is being initiated as to the registrations of products containing benzene hexachloride, lindane, chlordane, endrin, heptachlor and toxaphene, all products containing mercury, arsenic, or lead, and all others deemed necessary for review. The function of review is not to make another study of pesticides, but to identify which, if any, of the presently registered products present substantial questions of safety which should trigger the administrative process of cancellation." (Ruckelshaus, 1971)

In order to activate this review process, a Special Review Group was established by the Commissioner of the Office of Pesticides to set priorities and appoint working groups to study the individual pesticides in question. Accordingly, the first Working Group was established and assigned the task of:

(1) reviewing the currently registered uses of mercurial pesticides,

(2) evaluating these uses in terms of human safety and contamination of the environment, and

(3) based on this evaluation, making recommendations for cancellation of registrations which present a substantial question of safety or of environmental contamination.

*Basis for Approach* — In "Reasons Underlying the Registration Decisions Concerning Products Containing DDT, 2,4,5,-T, Aldrin and Dieldrin," (Ruckelshaus, 1971) the Environmental Protection Agency interpreted its responsibilities under the Federal Insecticide, Fungicide and Rodenticide Act and under the Food, Drug and Cosmetic Act as being required to:

(1) register new economic poisons if they meet certain standards of efficacy and safety, and

(2) undertake a continuous review of previously registered pesticides in order to insure continued compliance with these requirements in the light of the developing scientific data and concern for public health. If this continuing review *raises any substantial questions of safety, notices of cancellation must be issued* which initiate the administrative process of review.

In continuing to define the Agency's responsibilities, the document interprets the thrust of the Federal Insecticide, Fungicide and Rodenticide Act as prohibiting:

(1) those economic poisons which do not contain directions for use which are necessary and adequate for the protection of the public, and

(2) those economic poisons which do not contain a warning or caution statement which is adequate to prevent injury to man, vertebrate animals, or vegetation (except weeds).

The final decision with respect to whether a particular product should be registered initially or should continue to be registered depends upon the *intricate balance struck between the benefits and dangers* to public health and welfare resulting from its use. "The fact that the danger results solely from misuse does not determine that such danger is to be ignored but that this consideration has a possible bearing on the magnitude and possibility of occurrence of the risk." (Ruckelshaus, 1971, 6,10).

A product which has previously been registered may either be cancelled or suspended if the Administrator determines that the product does not comply with the provisions under which it was registered. The initial step in the administrative process, cancellation of registration, is triggered whenever the Administrator determines from all the data before him that there is a *substantial question as to the safety of a product*. The cancellation decision does not turn on a scientific decision alone. The statute leaves room to balance the benefits of a pesticide against its risks. In other words, the type, extent, probability, and duration of potential or actual injury to man, plants, and animals will be measured in the light of the positive benefits accruing from the responsible use of the pesticide. In its consideration of a specific pesticide usage, the Agency is mindful of its statutory directive and duty to the public to place the dictates of health and safety over economic considerations in its scale of values.

In the consideration of the term "safety" one must realize that this is never absolute (Mrak, 1969). Health risks assumed by an individual in his home or in the street are accepted as inevitable and may be limited to some extent by the individual. Health hazards stemming from environmental exposure to chemical agents are beyond the capacity of the individual to control. (Mrak, 1969).

In the consideration of "health" one must realize that this encompasses more than an absence of disease. Included is the feeling of well-being and capacity of happiness that derives from a suitable environment - suitable in the sense that makes possible the enjoyment of nature and her bountiful provisions of flora and fauna (Mrak, 1969).

Based on the above considerations, and as directed by the Agency, the Working Group will weigh the following criteria in determining the need for the continued registrations of specific uses of mercurial pesticides:

(1) the nature and magnitude of the foreseeable hazards associated with each specific use will be evaluated. These hazards may apply directly to human health, or to domestic plants and animals, or to wildlife, or to the environment generally;

(2) the nature of the benefit conferred by each use will be weighed. Some uses are obviously more important to public health and well-being than others. The nature of the benefit, if any, will be detailed;

(3) an attempt will be made to assess the magnitude of the social cost of foregoing any use recommended for cancellation; and

(4) alternatives for each use will be considered.

As the result of this review and the application of the above criteria, the Working Group will recommend the cancellation of the registration for those uses which, in its opinion, there is a substantial question of safety.

# RECOMMENDATIONS CONCERNING THE REGISTRATIONS OF MERCURIAL PESTICIDES

The Special Pesticide Review Group has reviewed and evaluated the registered uses of mercurial pesticides on a use-by-use, benefit-versus-risk basis. Based on this evaluation, the Special Pesticide Review Group makes the following recommendations concerning the continued registration of these pesticides.

RECOMMENDATION 1:

Suspend immediately the registrants for all pesticide products containing alkylmercury compounds.

The recommendation of suspension of all alkylmercury-containing pesticides is based on the high toxicity of these compounds to humans. The volatility and toxicity of the alkylmercuries present not only a hazard in the use of the pesticides containing these compounds but also an unnecessary hazard in their manufacture, formulation, and storage. The alkylmercuries have a propensity for accumulating in the brain and producing an insidious onset of symptoms associated with damage to the central nervous system. The registrations for seed dressings containing these compounds have been previously suspended. It is now considered that all other pesticides containing alkylmercury compounds present an "imminent hazard to the public" and their registrations should be suspended.

RECOMMENDATION 2:

In addition to the suspension recommended above, the Committee further recommends that in the absence of an imminent hazard finding, all other products containing mercury be cancelled except those intended for use as seed dressings for the prevention of stinking smut in wheat and leaf stripe smut in growing barley. The Group also recommends that the Administrator request the Secretary of Agriculture to develop alternative methods for the prevention of these diseases in wheat and barley. When this has been accomplished, the Environmental Protection Agency will cancel these two remaining uses of mercurial pesticides.

RECOMMENDATION 3:

Initiate monitoring activities to determine (1) the effect of the decreased use of mercury stemming from the cancellation of mercury-containing pesticides on the general level of mercury in the environment, and (2) the effect of the continued use of mercury-treated wheat and barley on the mercury levels in man and his environment in the regions in which these seeds are used.

RECOMMENDATION 4:

Continue research on the effects of mercury in the environment, especially in the areas of (1) development of more sensitive methods of determining the effects in humans of low level exposure to mercury; and (2) the biotransformation of mercury compounds.

RECOMMENDATION 5:

The nonpesticidal uses of mercury should be reviewed by the other components of the Agency with the goal of eliminating other sources of mercury contamination of the environment.

# SUMMARY

Although the toxic properties of mercury and its compounds have long been recognized, it is only recently that the impact on man and the environment of the extensive increase in industrial and agricultural uses has come to light. The first warnings of the hazard to the environment resulting from the agricultural use of mercury came from Sweden in the 1950's where the drastic decline in the populations of both seed-eating and raptorial birds was linked to mercury-treated seeds. At about the same time the effects of industrial pollution on humans became apparent in Japan where the first poisonings from mercury-contaminated fish occurred in Minamata in 1953. This was followed in 1965 by a similar occurrence in Niigata. Soon it was realized that mercury pollution of lakes and rivers from industrial pollution was also a serious problem in Sweden. In 1970 systematic surveys of fish and wildlife in both Canada and the United States led to the realization that North America was also faced with the mercury problem.

Human poisonings resulting from exposure during the manufacture, formulation, and use of mercurial pesticides or from the accidental ingestion of mercury-treated grain date as far back as the use of these pesticides, especially the alkylmercury pesticides. While the accidental ingestion of mercury-treated grain has resulted in many poisonings and deaths in foreign countries, it was not until the recent highly publicized incident in Alamogordo, New Mexico, in 1969 that the American public became aware of this potential hazard.

Inorganic and organic mercury are used in pesticides. The organic compounds that have gained importance all have the general structure R-Hg-X, where R is an organic radical, alkyl, alkoxyalkyl, or aryl. The group X is bound to mercury with a bond more or less having the character of a salt and originating from organic or inorganic substances with dissociable hydrogen ions, e.g. acids, amides, phenols, or thiols. At present, some one hundred combinations of different organic radicals and anions are used in commercial preparations of mercury fungicides.

All alkylmercury compounds used for seed treatments and all mercury compounds used as slimicides, algicides, and in laundries have previously been cancelled. The registrations of products containing hydroxymercurichlorophenol bearing directions for use on vegetable and field crop fields, the registrations of products containing hydroxymercurinitrophenol bearing directions for use on potatoes and sweet potatoes, and the registrations of products containing phenylmercuric acetate or phenylmercuric ammonium acetate bearing directions for use on apples, cherries, peaches, strawberries, and sugarcane have previously been cancelled as the result of implementing the NAS, NRC Advisory Committee recommendations to abolish "no residue" and "zero tolerance" registrations.

Inorganic and arylmercury compounds are more acutely toxic than the alkyl compounds. The arylmercuries are relatively rapidly degraded in the body to inorganic mercury, and their tissue distribution resembles inorganic mercury. Accumulation of mercury from these compounds is mainly in the liver and kidneys. The placenta is an effective barrier to the entry of these compounds. In addition, they are rapidly excreted in the urine and feces. In contrast, the alkylmercuries are better absorbed, show a more even tissue distribution and are more slowly metabolized. They readily cross the "blood-brain barrier" in man. They are able to cross the placental barrier, where accumulation in the fetus may exceed that in

maternal tissues and may cause fetal neurological damage. All of the compounds of mercury are capable of causing chromosomal aberrations. This effect is more marked with the alkyl and aryl compounds than with inorganic mercury.

A complicating feature of the mercury problem was the discovery that mercury in river and lake bottoms can be converted into methylmercury. This biotransformation is responsible for the contamination of aqueous systems and their associated biota. Indirectly, this process may also play, through the evaporation of dimethylmercury, a role in the atmospheric transport of mercury. In addition, microbial systems in the interstinal flora of birds and mammals may be involved in the methylation of mercury.

Because of its volatility, mercury normally circulates in the environment between the soil and water and the atmosphere. Man's use of mercury has added to this natural circulation by increasing the concentration in the atmosphere over the years through the burning of fossil fuels and the smelting of ores. Man has also produced areas of abnormally high concentrations of mercury through industrial wastes and the use of mercurial pesticides. The pollution of rivers and lakes with mercury from the effluents of industrial plants has been abated. However, the pesticidal use of mercury remains as the largest intentional dissipative or nonrecyclable use of mercury in the United States.

# CHAPTER I

# THE PESTICIDE USES OF MERCURY

## Introduction

Because of incomplete records and the fact that specific uses for products registered "For manufacturing use" can not always be identified, we are not certain that we have identified all pesticide uses of mercury or all available substitutes. It is estimated that the following outline covers approximately 98% of all such uses.

The classification of uses is arbitrary and is usually based on label claims which are often so general in nature as to prohibit specific identification.

According to figures produced by the Bureau of Mines, about 986,252 lb of metallic mercury were used in the production of pesticides in 1969. This included production of products from imported mercury and other sources.

## Summary and Conclusions

There is a serious lack of information on nonagricultural uses of mercury-containing pesticides, and data are not available for a proper evaluation of the economic impact of the withdrawal of such uses.

Mercury compounds presently registered include alkyl, aryl and inorganic types. All alkylmercury compounds used for seed treatments and all mercury compounds used as slimicides, algicides and in laundries have previously been cancelled and are not included in this report. The remaining uses involve many different commercial, household, industrial and institutional applications. Uses requiring the largest amounts of mercury include paints, seed treatments and turf disease control.

A careful review of registrations of nonmercurial products indicates that no substitutes are currently registered for the following uses:

(1) barley - seed treatment for stripe disease

(2) broomcorn - for mildew control

(3) cellulose sponges - preservation

(4) sacks, bins and containers for treated seed - fungus and bacterial plant disease organisms

(5) seam and bedding compounds used in boat construction

(6) textures and other dry products ultimately applied by dispersion in water

(7) elm trees (by injection) - Dutch Elm Disease

(8) wheat - seed treatment - seed-borne phase of smut control.

It is also recognized that, although substitute materials appear to be available for all other uses, the general patterns described on many product labels preclude an accurate assessment of individual applications in specific formulations or processes. Thus, substitute materials may not be available for all paint formulations, certain tanning processes or other uses. Conversely, the fact that no substitute is presently registered for a specific formulation or process does not mean that one is not known which can be registered for such use.

## I. Coatings

### 1. Adhesives

#### A. Mercury compounds

Phenylmercuric acetate: [Ref. I-P-08-00.09]
For preservation of product: 45 to 250 ppm
For mildew control after application: 3500 to 15,000 ppm based on total wet weight.

#### B. Substitute compounds

(1) Alkyl dimethyl benzyl ammonium chloride: [Ref. I-A-08-45.05] fungistat: 800 ppm by weight. [Ref. I-A-08-50.01] preservative: 50,000 ppm plus other fungistats.

(2) Bis (tributyltin) oxide: [Ref. I-D-09-00.02] fungistat: use in amount required.

(3) 4-Chloro-3, 5-xylenol: [Ref. I-C-21-00.02] fungistat: use as required.

(4) Dehydroabietylamine pentachlorophenate: [Ref. I-D-02-00.01] fungistat: 1700 to 8000 ppm by weight of adhesive.

(5) Hexahydro-1, 3, 5-triethyl-s-triazine: [Ref. I-H-04-00.01] fungistat: 100 ppm by weight.

(6) Monoethanolammonium 2-mercaptobenzothiazole: [Ref. I-M-21-00.01]

(a) 2000 to 4000 ppm for low protein adhesives by weight.

(b) 800 to 12,000 ppm for high protein adhesives by weight.

(7) Parachlorometacresol: [Ref. I-P-01-00.01] fungistat: 500 to 1500 ppm by weight of product.

(8) Sodium o-phenylphenate: [Ref. I-S-16-00.08] preservation: 500 to 1000 ppm by weight.

(9) Vinylene bisthiocyanate: [Ref. I-V-01-00.01]

(10) Tetrahydro-3, 5-Dimethyl-2H-1, 3, 5-thiadiazine-2-thione (Mylone): [Ref. I-T-07-00.01] 0.01 to 0.5% by weight of suspension.

(11) Ziram: [Ref. I-Z-11-00.07] (1) plus zinc-2-mercaptobenzothiazole (2) 180 ppm (1) plus 20 ppm (2) to 2300 ppm (1) plus 50 ppm (2) by weight.

#### C. Comparative effectiveness and impact

(1) In general, mercury compounds are effective at lower dosages and against a broader spectrum of fungi than are the substitute materials.

(2) Impact of withdrawal of mercury uses as pesticides in adhesives should be minimal.

### 2. Coatings for outdoor fabrics

#### A. Fungistatic:

(1) *Mercury compounds*
Phenylmercuric oleate [Ref. I-P-14-00.0] 500 to 5000 ppm by weight of coating.

(2) *Substitute compounds*

(a) None specifically identified by label claims but might include products used in sealers and sizings, and certain plastics.

(b) Bis (tributyltin) oxide: [Ref. I-S-09-00.02] For furniture and similar items (vinyl) 4,000 to 10,000 ppm by weight of nonvolatile components of formulation.

(3) *Comparative effectiveness and impact*

(a) Comparative effectiveness unknown.

(b) Impact of withdrawal of mercury for this use on industry and consumer is also unknown.

#### B. Bacterial preservatives:

(1) *Mercury compounds*
Phenylmercuric hydroxide 17% (powdered): [Ref. 6516-3]
Paint (unspecified) coatings for fabrics: 0.5 lb product per 99.5 lb media.

(2) *Substitute compounds*

(a) Alkyl (50%$C_{12}$, 30%$C_{14}$, 17%$C_{16}$, 3%$C_{18}$) dimethyl ethylbenzyl ammonium cyclohexylsulfamate (80%): [Ref. 1839-36] 0.1% to 0.2% product by weight.

(b) 1-(30chloroallyl)-3, 5, 7-triaza-1-azoniadamantave chloride (90%): [Ref. 464-327]

(a) latex paints: 2000 ppm product.

(b) polyvinyl acetate latex: 250 ppm product.

(c) Sodium 2-pyridinethiol 1-oxide (40%): [Ref. 1258-843] 1.15 lb product/10,000 lb emulson, 115 ppm product.

(d) Captan (N-trichloromethylthio-4-cyclohexene-1, 2-dicarboximide) (90%): [Ref. 1965-11]
0.2% to 0.5% product by weight of total formula.

(e) Alkyl (5% caprylyl, 7% capryl, 56% lauryl, 18% myristyl, 7% palmityl, 5% stearyl, 2% linoleyl) hydrochlorides (25%): [Ref. 8489-13]
0.15% to 0.3% product based on total weight of composition.

(3) *Comparative effectiveness and impact*

A. Mercury compounds are colorless. Some substitute chemicals impart undesirable colors.

B. Substantivity of some substitute chemicals to fabric greater than mercury compounds.

C. Substitute chemicals appear to be adequate.

D. Impact on industry expected to be minimal. Increase in costs to consumer expected.

3. **Cements and plasters** (see also 7)

A. **Fungistatic**

(1) *Mercury compounds*
Phenylmercuric acetate: [Ref. 1-P-08-00.09] For preservation: 45 to 250 ppm by dry weight. For fungistat after application: 3500 to 15,000 ppm.

(2) *Substitute compounds*
Bis (tributyltin) oxide: [Ref. 1-B-09-00.02] Tape-joint compounds: 150 ppm by weight.

(3) *Comparative effectiveness and impact*

(a) Bis (tributyltin) oxide is generally comparable in effectiveness to PMA. Other substitute materials are probably available but cannot be identified specifically from label claims.

(b) Impact of withdrawal of mercury for this use should be insignificant.

B. **Cement (bacterial preservative)**

(1) *Mercury compounds*
Phenylmercuric acetate (95%) powder: [Ref. 6515-7] 2 ounces product per bag of cement (size not specified).

(2) *Substitute compounds*

(a) 2, 3, 5, 5-Tetrachloro-4-(methylsulfonyl) pyridine (82%): [Ref. 464-353] 1.0% to 2.0% product by weight of formulation.

(b) Sodium pentachlorophenate (79%): [Ref. 464-125] 1.0% product by weight in water: 0.5% to 3.0% of solution by weight of product in which incorporated.

(c) Dehydroabietylamine pentachlorophenate (40%): [Ref. 2829-56] 0.5% to 2% product by weight of media.

(3) *Comparative effectiveness and impact*

(a) Other chemical compounds, although not specifically recommended for this application, may also be used.

(b) Substitute compounds appear to be adequate.

(c) Impact on industry may be significant in that sufficient substitute compounds for a variety of building applications may not be available. Impact on consumer may also be significant where preservation against bacteria in humid climates is a necessity. Mercurials have had a long history of use in building applications and are known to be highly effective.

4. **Paints**

A. **Antifouling marine coatings**

(1) *Mercury compounds*

(a) Mercuric oxide: [Ref. Reg. No.

2693-57, 2693-20]

(aa.) 0.5 to 6.0%, in combination with 3.75% cuprous oxide and 1.4 to 6.5% "mercury phenate."

(bb.) 0.5 to 6.0%, in combination with 17.5% cuprous oxide.

(c) Mercury phenate:
1.4 to 6.5%, in combination with mercuric oxide (see 4 A (a) above)

(d) Phenylmercuric acetate: [Ref. Reg. Nos. 3073-17, 25, and 26] 4.5%, used alone.

(e) Phenylmercuric oleate: [Ref. Reg. Nos. 539-214, 215, 216 and 218]

(aa.) 0.95 to 1.11%, used alone, or

(bb.) 0.89% in combination with 23,88% metallic copper.

(2) *Substitute compounds*

(a) Copper (metallic): [Ref. Reg. Nos. 8120-3 and 9792-1] 15.0 to 48.2% by weight.

(b) Copper acetoarsenite: [Ref. Reg. Nos. 390-11 and 390-38] 16 to 26.5% in combination with 13.5% copper powders or 2.0% Bis (tributyltin) oxide.

(c) Copper hydroxide: [Ref. Reg. Nos. 3073-2 and 3073-34] 8 to 9% in combination with 48% copper oxide or 24% copper oxide.

(d) Copper linoleate: [Ref. Reg. No. 2693-47] 9.4% in combination with 31.5% cuprous oxide.

(e) Copper oleate: [Ref. Reg. Nos. 9461-50 and 9461-48] 3.4 to 8.0% in combination with 38.9 percent cuprous oxide or 10% cuprous oxide.

(f) Copper resinate: [Ref. Reg. No. 2568-7] 3% in combination with 16.8% cuprous oxide plus 12.6% capric acetoarsenite plus 1.4% pine oil.

(g) Cuprous oxide: [ref. Reg. Nos. 10250-1 and 3658-2] 7.5 to 74.5% alone

(h) Bis (tributyltin) oxide: [Ref. Reg. Nos. 390-30 and 568-20] 4.6 to 10% alone.

(i) Dichlone: [Ref. Reg. No. 3658-3] 5.5 percent in combination with 51.2% cuprous oxide.

(j) Pentachlorophenol: [Ref. Reg. No. 9461-52] 2.23% in combination with 24.59% cuprous oxide plus 1.86% Bis (tributyltin) oxide.

(k) Phenarsaxine chloride: [Ref. Reg. Nos. 2693-35 and 2693-36] 4.5 to 6.4% in combination with 19.4% cuprous oxide or 31.5% cuprous oxide.

(l) Tributyltin fluoride: [Ref. Reg. Nos. 3658-14 and 8019-13] 5.55 to 14.3% alone.

(3) *Comparative effectiveness and impact*

(a) Substitute compounds are effective replacements for mercury in marine finishes.

(b) Impact of withdrawal of mercury from these uses will be insignificant.

B. **Paints (bacterial preservative)**

(1) *Mercury compounds*
Phenylmercuric oleate (30%): [Ref. Reg. Nos. 6516-10 and 8489-1]

(a) 2 ounce by weight packet to 1 gal of oil - based paint, application to marine surfaces on pleasure craft.

(b) 0.5 lb product/100 gal finished formula.

(2) *Substitute compounds*

(a) 2, 3, 4, 6-Tetrachlorophenol (74%): [Ref. Reg. No. 464-71] 1.0% to 3.0% product by weight of formulation.

(b) 2, 3, 5, 6-Tetrachloro-4-(methylsulfonyl) pyridine (82%): [Ref. Reg. No. 464-333]

(aa.) Oil-based high zinc content: 0.25% to 0.5% by weight of formulation.

(bb.) Zinc-oxide free systems: 1 to 3% to weight of formulation.

(cc.) Interior paints: flat finishes - 0.3%; gloss paints 0.7% by weight of formulation.

(c) 2-(Thiocyanomethylthio) benzothiazole (32%) and 2-Hydroxypropyl methanethiosulfonate (28%): [Ref. Reg. No. 1448-27]

(aa.) Oil paint, zinc oxide: 0.1 to 0.5% by weight of formulation.

(bb.) Oil paint, zinc-free alkyd: 0.3 to 1.0% by weight of formulation.

(3) *Comparative effectiveness and impact*

(a) Some substitute compounds impart odors to finished paint film that may be undesirable in food processing areas.

(b) Listed substitute compounds cannot be considered inclusive. Paint preservative compounds used for water-based paints or synthetic emulsion-type paints may also be substituted.

(c) Substitute compounds appear to be adequate.

(d) Impact on industry expected to be small, impact on consumer expected to be negligible.

5. **Paints, varnishes, stains**

A. **Fungistatic (mildew control)**

(1) *Mercury compounds*

(a) Chloromethoxy-acetoxymercuripropane: [Ref. I-C-14-00.01] Mfg. use label, no directions for use.

(b) Di (phenylmercury) dodecylsuccinate: [Ref. I-D-21-00.01]

(aa.) Household use: 3750 ppm added to paint.

(bb.) Industrial use: add in amount required.

(c) Phenylmercuric acetate: [Ref. I-P-08-00.09]

(aa.) Preservation: 0.1 to 0.25 lb/100 gal.

(bb.) Mildew control: 1.0 to 3.0 lb/100 gal.

(cc.) Preservation of protein colloid components: 0.23 to 0.3 lb/100 gal.

(dd.) Preservation of carbohydrate components: 0.1 to 0.15 lb/100 gal.

(d) Phenylmercuric borate: [Ref. I-P-08-10.01] Mold control: 0.2 to 3.0 lb/100 gal.

(e) Phenylmercuric hydroxide: [Ref. I-P-09-50.01] Aqueous systems: 4500 to 9000 ppm residual in coating.

(f) Phenylmercuric oleate: [Ref. I-P-14-00.01 and .02]

(aa.) Mildew on paint film, decay on stained surfaces as household or commercial use: 1200 ppm plus 14,250 ppm of pentachlorophenol added to coating.

(bb.) Industrial use:
333 to 1666 ppm by weight of coating: 1.0 to 6.66 lb actual/100 gal.

(g) Phenylmercury propionate: [Ref. I-P-1500.01] Mildew control: 1.5 to 4.0 lb actual/100 gal.

(2) *Substitute compounds*

(a) Alkyl dimethyl benzyl ammonium chloride: [Ref. I-A-08-25.06] Mildew control: aqueous systems—366 ppm plus 610 ppm TBTO.

(b) Alkyl dimethyl ethybenzyl ammonium cyclohexyl sulfamate: [Ref. I-A-17-00.01] Aqueous exterior systems (latex): 600 to 800 ppm by weight.

(c) Barium metaborate: [Ref. I-B-01-00.91]

(aa.) 8.35% by weight of paint.

(bb.) 0.09 to 0.36% by weight for preservation of finished colors containing protein.

(cc.) 0.09 to 0.27% by weight for preservation of finished colors containing carbohydrates.

(d) trans-1, 2-Bis (propylsulfonyl) ethene: [Ref. I-B-07-80.01] 3000 to 5000 ppm by weight—for oil-based paints.

(e) Bis (tributyltin) oxide: [Ref. I-B-09-00.01 and .02]

(aa.) Household use in aqueous systems: 610 ppm by volume.

(bb.) Industrial use: 500 to 1000 ppm by weight of polyvinyl acetate formulations;
1500 to 3000 ppm by weight of acrylic formulations;
2500 to 3500 ppm by weight of styrenebutadiene formulations:
0.92 lb/100 gal of interior paint;
6 to 9 lb/100 gal of exterior paint;
8 to 12 lb/100 gal of roof paint.

(f) Captan: [Ref. I-C-10-00.15 and .16]

(aa.) Household uses: 1.0 oz/gal of oil-based paint.

(bb.) Industrial use: 3600 to 9000 ppm by weight of paint.

(g) 4-Chloro-3, 5-xylenol: [ref. I-C-21-00.01 and .02]

(aa.) Household use: 1.0 fluid oz of 45% solution/gal of interior, oil or emulsion formulations.

(bb.) Industrial use: in amounts required.

(h) Copper 8-quinolinolate: [Ref. I-C-34-00.01 and .02]

(aa.) Commercial use: 0.75 pint of 10.0% solution/gal.

(bb.) 10,000 ppm by weight of solids or by total weight of paints, varnishes or sealers.

(i) Parachlorometacresol: [Ref. I-P-01-00.01] 500 to 1500 ppm by weight of aqueous system paints.

(j) Potassium o-phenylphenate: [Ref. I-P-26-00.01]

(aa.) Preservation: 0.15 to 2.0 percent by weight.

(bb.) Mildew control: 10,000 to 20,000 ppm by weight of polyvinyl acetate formulation.

(k) Potassium 2, 4, 6-trichlorophenate: [Ref. I-P-28-80.01] Mildew control: 3750 to 22,500 ppm by weight.

(l) Sodium o-phenylphenate: [Ref. I-S-16—00.09]
Preservation: 2000 to 5000 ppm by weight of oil- or water-based formulations.

(m) 2, 3, 5, 6-Tetrachloro-4-methylsulfonyl pyridine: [Ref. I-T-02-00.01] 500 to 30,000 ppm by weight of alkyl, latex or oil formulations.

(n) Tetrahydro-3, 5-dimethyl-2H-1, 3-, 5-thiadiazine-2-thione: [Ref. I-T-07-00.03]

(aa.) Interior paint - mildew: 1000 to 20,000 ppm by weight of paint.

(bb.) Aqueous components molds: 100 to 5000 ppm. by weight of suspension.

(o) 2-(4-Thiazolyl) benzimidazole: [Ref. I-T-09-00.02 and .03]

(aa.) Exterior paints:
0.25 to 2.0 lb/100 gal.

(bb.) Interior paints:
0.1 to 1.0 lb/100 gal.

(p) 3, 4', 5-Tribromosalicylanilide: [Ref. I-T-11-00.02] 1000 ppm by weight of butadiene - styrene latex formulation.

(q) Tributyltin salicylate: [Ref. I-T-12-80.01] Amount as required.

(r) Zineb: [Ref. I-Z-10-00.14]
Household use: 1.0 to 1.5 ounces/gal.

(3) *Comparative effectiveness and impact*

(a) Very little is known about the comparative effectiveness of mercury and substitute compounds in paints. Mercury is compatible with most types and formulations of both oil- and water-based types. Most substitute compounds are limited as to type of paint and specific formulation in which they can be used or that has been tested.

(b) The industry recognizes the need to develop substitute materials but has indicated that time is needed to test compounds now available.

(c) The impact of withdrawal of mercury from the pesticide uses in paints, varnishes and lacquers would be very severe on the manufacturers and could leave the public in a "distress situation" in regard to mildew control on paint films, particularly in areas with severe mildewing conditions.

B. **Paint and premanufactured paint components preservation (bacteriostatic):**

(1) *Mercury compounds*
Phenylmercuric acetate (100% powder): [Ref. Reg. No. 8489-5]

(a) Preservative for polyvinyl acetate, acrylic and butadiene-s styrene systems. Package stability for aqueous systems such as paint and carbohydrate thickener solutions: 2 to 4 ounces product/100 gal media by weight.

(b) Preservation of protein colloids and systems containing same: 4 to 8 ounces product/100 gal media by weight.

(2) *Substitute compounds*

(a) Sodium pentachlorophenate (79%): [Ref. Reg. No. 464-299] 0.1% to 0.2% product by weight of particular substrate.

(b) 1-(3-chloroallyl)-3, 5, 7-triaza-1-azoniaadamatane chloride (90%): [Ref. Reg. No. 464-327]

(aa.) Aqueous paint systems: 0.1% to 0.2% product by weight of formulation.

(bb.) Paint components: 0.05% to 0.15% product by weight of media.

(c) Sodium 2, 4, 5-trichlorophenate (85%): [Ref. Reg. No. 464-131] For preservation of polyvinyl acetate emulsions:0.4% product by weight of media.

(d) Sodium o-phenylphenate: [Ref. Reg. No. 464-78] Preservation of carbohydrate thickener solutions: 0.05% to 0.2% product by weight of media.

(e.) 50:50 mixture o-phenylphenol and Pentachlorophenol: [Ref. Reg. No. 464-70 and 464-72]

0.5% of mixture based on weight of wet formulation for preservation of protein colloids.

(f) Sodium 2-pyridinethiol 1-oxide (2%): Ref. Reg. No. 1258-846] Preservation of acrylic latex paint, 0.25% product by weight of formulation.

(g) 2-(Thiocyanomethylthio) benzothiazole (32%) and 2-Hydroxypropyl methanethiosulfonate (28%): [Ref. Reg. No. 1448-27]

Alkyl-modified emulsion paint preservative: 0.3% to 1.0% product by weight of formulation.

(h) Alkyl (50%$C_{12}$, 30%$C_{14}$, 17%$C_{16}$, 3%$C_{18}$) dimethyl ethylbenzyl ammonium cyclohexylsulfamate (80%): [Ref. Reg. No. 1839-36]

(aa.) Latex paint preservative: 0.1% to 0.2% product by weight of paint.

(bb.) Carbohydrate and protein colloid preservative: up to 0.1% product by weight of formulation.

(i) Dehydroabietylamine pentachlorphenate (50%): [Ref. Reg. No. 2829-59] Water-based paint preservative: 0.35% product based on finished weight of formulation.

(j) Alkyl (5% caprylyl, 56% lauryl, 18% myristyl, 7% palmityl, 5% stearyl, 2% linoleyl) hydrochlorides (25%): [Ref. Reg. No. 8489-13] Preservation of water-containing and emulsion-type adhesives, Paints and their components: 0.15% to 0.3% product based on total weight of composition.

(k) 1, 2-benzisothiazolin-3-one (23%): [Ref. Reg. No. 10182-1] Preservation of water-based paints, emulsion paints and components: [0.15% product based on total weight of paint.

(3) *Comparative effectiveness and impact*

(a) Mercury compounds can cause "browning" of certain paint formulations, substitute compounds much less so.

(b) Some substitute compounds impart objectionable odor to finished paint film.

(c) Substitute compounds appear to be adequate.

(d) Impact on industry expected to be negligible, price of end-product to consumer expected to rise.

C. **Latex vinyl paint finish on asbestos ceiling tile (bacteriostatic and self-sanitizing against bacteria)**

(1) *Mercury compounds*

(a) Phenylmercuric acetate (0.0034% to 0.004% by weight of total product): [Ref. Reg. Nos. 7816-3, 8700-2] Product is component of tile vinyl latex paint applied at rate of 3.13 gal paint per 100 sq ft. of ceiling tiles or panels, equal to 0.02 lb phenylmercuric acetate per 1000 sq ft.

(b) Phenylmercuric propionate (0.0013% to 0.005% by weight of total tile): [Ref. Reg. Nos. 7850-11, *et al*]

Product is component of vinyl latex paint applied to asbestos ceiling tile. Bears bacteriostatic (bacterial growth inhibiting) and self-sanitizing (reduction of bacterial numbers) claims; used primarily in hospitals and nursing homes.

(c) Chloromethoxypropylmercuric acetate (0.002% based on total weight of tile) and copper pentachlorophenate (0.02%): [Ref. Reg. No. 10591-1]
Product component of white latex paint and clay primer applied to ceiling tile and wallboard applied at rate of 0.013 pounds product (in latex paint) per 1000 square feet of surface.

(2) *Substitute compounds*

(a) 1-(3-chloroallyl)-3, 5, 7-triza-1-azoniaadamantane chloride (90%): [Ref. Reg. Nos. 464-327]
0.1% to 0.2% product by weight of formulation.

(b) 2, 3, 5, 6-Tetrachloro-4-(methylsulfonyl) pyridine (82%): [Ref. Reg. No. 464-353]
0.5 to 1.0% by weight of formulation.

(c) Captan (N-trichloromethylthio-4 cyclohexene-1, 2-dicarboximide) (90%): [Ref. Reg. No. 1965-11]
0.25% to 1.0% product by weight of formulation.

(d) Alkyl (5% caprylyl, 7% capryl, 56% lauryl, 18% myristyl, 7% palmityl, 5% stearyl, 2% linoleyl) hydrochlorides (25%): [Ref. Reg. No. 8489-13]
0.15 to 0.3% product on total weight of media.

(e) Phenol (1.41%), Sodium borate (0.47%) and Sodium phenate (0.24%): [Ref. Reg. No. 8383-1] 2% to 5% by weight of active ingredients.

(f) 2-(Thiocyanomethylthio) benzothiazole (32%) and 2-Hydroxypropyl methanethiosulfonate (28%): [Ref. Reg. No. 1448-27]
0.03 to 0.05% product based on formula weight.

(g) Alkyl ($50\%C_{12}$, $30\%C_{14}$, $17\%C_{16}$, $3\%C_{18}$) dimethyl ethylbenzyl ammonium cyclohexylsulfamate (80%): [Ref. Reg. No. 1839-36]
0.1 to 0.2% product by weight of formulation.

(3) *Comparative effectiveness and impact*

(a) Comparative costs of substitutes and mercury compounds not known.

(b) Substitute compounds appear to be adequate.

(c) Impact on industry expected to be minimal, consumer impact somewhat variable.

(d) Impact on uses of product in critical hospital areas requiring low bacterial counts cannot be assessed.

### D. Vinyl latex interior paint (bacteriostatic finish)

(1) *Mercury compounds*
Phenylmercuric acetate: [Ref. Reg. No. 10751-1]
Component of paint, 0.27% by weight.

(2) *Substitute compounds*

(a) Phenol (1.4%) and Sodium borate (0.47%), and Sodium phenate (0.24%): [Ref. Reg. No. 8383-1]
2 to 5% by weight of active ingredients.

(b) 1-(3-chloroallyl)-3, 5, 7-triaza-l-azoniaadamantane chloride (90%): [Ref. Reg. No. 464-327]
0.1 to 0.2% product by weight of formulation.

(c) Sodium 2-pyridinethiol-1-oxide (90%): [Ref. Reg. No. 1258-842]

(aa.) 0.5 lb/10,000 lb formulation.

(d) Captan (N-trichloromethylthio-4 cyclohexene-1, 2-dicarboximide) (90%): [Ref. Reg. No. 1965-11]
0.25 to 1.0% product by weight of paint.

(e) Alkyl (5% caprylyl, 7% capryl, 56% lauryl, 18% myristyl, 7% palmityl, 5% stearyl, 2% linoleyl) hydrochlorides (25%): [Ref. Reg. No. 8489-13] 0.15 to 0.3% product based on total weight of media.

(f) 2-(Thiocyanomethylthio) benzothiazole (32%) and 2-Hydroxypropyl methanethiolsulfonate (29%): [Ref. Reg. No. 1448-27] 0.03 to 0.05% product based on formula weight.

(g) Alkyl ($50\%C_{12}$, $30\%C_{14}$, $17\%C_{16}$, $3\%C_{18}$) dimethyl ethylbenzyl ammonium cyclohexylsulfamate (80%): [Ref. Reg. No. 1839-36]

0.1 to 0.2% product by weight of formulation.

(h) 2, 3, 5, 6-Tetrachloro-4-(methylsulfonyl) pyridine (82%): latex media: [Ref. Reg. No. 464-353]
0.5 to 1.0% product by weight latex media.

(3) *Comparative effectiveness and impact*

(a) Substitute compounds appear to be adequate.

(b) Impact on industry and consumer appear to be minimal.

### 6. Sealers and Sizings

#### A. Mercury compounds

(1) Phenylmercuric acetate: [Ref. I-P-08-00.09]

(a) Preservation: 0.1 to 0.25 lb/100 gal.

(b) Mildew control: 1 to 3 lb/100 gal.

(c) Preservation of carbohydrate solutions: 0.1 lb/100 gal.

(d) Preservation of protein solutions: 0.23 to 0.3 lb/100 gal.

(2) Phenylmercuric oleate: [Ref. I-P-14-00.01] mildew control: 1200 ppm by weight of formulation.

#### B. Substitute compounds

(1) Alkyl dimethyl benzyl ammonium chlorides: [Ref. I-A-08-45.05]
Preservation: 50,000 ppm plus other fungistats.

(2) 4-Chloro-3, 5-xylenol: [Ref. I-C-21-00.02] As required.

(3) Copper 8-quinolinolate: [Ref. I-C-3400.02] 1.0% by weight.

(4) Monoethanolamine 2-mercaptobenzothiazole: [Ref. I-M-21-00.01] 0.15 to 0.4% by weight.

(5) Sodim o-phenylphenate: [Ref. I-S-16-00.10] 2.0% by weight.

(6) Tetrahydro-3, 5-dimethyl-2H, -1, 3, 5-thiadiazine-2-thione (Mylone): [Ref. I-T-07-00.03]
100 to 5000 ppm by weight.

#### C. Comparative effectiveness and impact

(1) Substitute compounds are generally less effective than mercury at comparable dosage rates.

(2) Mercury compounds are less expensive and adapted to use in a wider range of products than are substitutes.

(3) Impact of withdrawal of mercury for these uses should have slight to moderate effect on manufacturers and consumers.

### 7. Textures and other dry products ultimately applied by dispersion in water (see also I. 3 cements and plasters).

#### A. Mercury compounds

Phenylmercuric acetate: [Ref. I-P-08-00.09]

(a) Preservation: 45 to 250 ppm by weight.

(b) Mildew control: 3500 to 15,000 ppm by weight.

#### B. Substitute compounds

None identified.

### 8. Wallpaper coatings

#### A. Mercury compounds

Di(phenylmercury) dodecenylsuccinate: [Ref. I-D-21-00.01]
Add to deposit 0.01 ounce of a 10.5 or 12.0% product/square yard of finished paper.

#### B. Substitute compounds

(1) 3, 4, 5-Tribromosalicylanilide( [Ref. I-T-11-00.02]
Incorporate 0.1% into plastic laminate before calendering.

(2) See additional probable substitutes under IX - Plastics.

#### C. Comparative effectiveness and impact

(1) Substitute compounds must be employed at higher concentrations than mercury to achieve comparable fungistasis.

(2) Mercury has a broader spectrum of fungal control than most substitute compounds.

(3) Impact of withdrawal of mercury for this use would appear to be slight.

## II. Fabrics and Textiles

### I. Fungistats

#### A. Mercury compounds

(1) Phenylmercuric acetate: fungistat for mildew control: industrial use in finishing processes. [Ref. I-P-08-00]

(a) 25 to 180 ppm in final rinse.

(b) 30 to 90 ppm by padding.

(c) 150 to 225 ppm by spraying.

(2) Phenylmercuric borate and chloride: fungistat, industrial use in finishing process. [Ref. I-P-08-10.01] 2.0 lb of a 1.1% PMB plus 0.10% PMC soln./100 gal in finishing bath = 26.5 ppm PMB plus 2.4 ppm PMC.

(3) Phenylmercuric oleate: fungistat: consumer use on awnings, boat covers, navy tops, curtains, sail covers. [Ref. I-P-14-00]

(a) 2000 to 2800 ppm alone or with TBTO and zinc naphthenate, by brush.

(b) coatings for outdoor fabrics: 0.05 to 0.5% of a 30% product, based on weight of coating. [Ref. I-P-14-00.02]

(4) Phenylmercuric propionate: fungistat: industrial use in finishing process. [Ref. I-P-15-00] 250 to 500 ppm by impregnation.

(5) Phenylmercuric triethanol ammonium lactate: fungistat for mildew, rot and decay: industrial use in finishing process. [Ref. I-P-17-00] 560 to 1130 ppm by impregnation or in size.

(6) Pyridyl mercuric chloride: (0.06% plus 7.5%) alkyl dimethyl benzyl ammonium chloride: industrial use in finishing process. [Ref. I-A-08-10.02] 1.2 to 1.3% of mixture retained on fabric by padding.

#### B. Substitute compounds

(1) Alkyl amine salts of tetrachlorophenol (alone or with TBTO): fungistat: industrial use in finishing process. [Ref. I-A-06-00.01]

(a) cotton, sisal, jute, hemp and similar materials: 10,000 to 20,000 ppm alone or 1090 ppm plus 210 ppm TBTO.

(b) carpet underlay: 1500 ppm plus 250 ppm TBTO.

(2) Alkyl dimethyl benzyl ammonium chlorides: fungistat: industrial processes.

(a) padding to retain 1.2 to 1.3% by weight of a mixture of quaternary plus o-phenylphenol and 2, 3-thiobis (4-chlorophenol). [Ref. I-A-08-10.02]

(b) 1500 to 6000 ppm quaternary by finishing equipment. [Ref. I-A-08-15.02]

(c) 5000 ppm quaternary plus 250 ppm TBTO by spraying. [Ref. I-A-08-15.02]

(d) 500 to 2500 ppm quaternary plus 150 to 500 ppm TBTO by padding or other suitable equipment. [Ref. I-A-08-15.02]

(3) Ammonium hydroxide $C_8$ fatty acid-silver complex: fungistat: consumer use. [Ref. I-A-25-00.01] 800 ppm spray.

(4) Bis (tributyltin) oxide: fungistat: industrial use in finishing process. [Ref. I-B-09-00.03]

(a) 250 to 500 ppm on clothing, etc.

(b) 500 to 1000 ppm on awnings, etc.

(5) Captan: fungistat: industrial use in finishing process. [Ref. I-C-10-00.16] Deposit 0.90 to 1.7% by weight of fabric.

(6) 4-or 6-chloro-2-phenylphenol: fungistat: consumer use. 2000 ppm spray, sponge or dip. [Ref. I-C-18-00.01]

(7) 4-chloro-3, 5-xylenol: fungistat: consumer use. [Ref. I- -21-00] 1200 ppm alone or 600 to 2000 ppm in combination with other fungistats.

(8) Copper 8-quinolinolate: fungistat: industrial use in finishing process. [Ref. I-C-34-00.03] 0.02 to 1.0% metallic copper equivalent deposited. Note: objectionable color for many types of fabric.

(9) Dehydroabiethylamine salt of pentachlorophenate: Industrial use in finishing process. [Ref. I-D-02-00.01]

(a) indoor fabrics: 0.25 to 1.25% by weight of fabric.

(b) outdoor fabrics: 0.8 to 1.5% by weight of fabric.

(10) Dialkyl dimethyl ammonium chloride: fungistat: industrial use in finishing process. [Ref. I-D-04-20.02] Deposit 28.1 to 3750 ppm quaternary plus 142.5 to 1250 ppm TBTO by weight.

(11) Diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride: fungistat: industrial use in finishing process. [Ref. I-D-13-00.04] 1635 to 2045 ppm quaternary plus 468 to 585 ppm tributyltin benzoate by weight of fabric.

(12) Dodecyl-di (beta-hydroxyethyl) benzyl ammonium chloride: fungistat: industrial use in finishing process. [Ref. I-D-26-10.01] For suitings, linings, blankets, upholstery fabrics, carpets and other articles seldom, if ever, laundered. 0.2 to 1.0 gram/liter of water by exhaustion or padding.

(13) N-Dodecylquanidine terephthalate: fungistat: industrial use in finishing process. [Ref. I-D-27-90.01] For awnings, tents, tarpaulins, sails and similar textiles: 2500 to 5900 ppm by padding.

(14) Lauryl pyridinium salt of 5-chloro-2-mercaptobenzothiazole: fungistat: industrial use in finishing process. [Ref. I-L-01-00.01]

(a) For burlap: 3375 to 10,000 ppm.

(b) Duck, mattress ticking, similar fabrics: 1250 plus 2500 ppm.

(c) Industrial fabrics and yarns: 5000 plus 10,000 ppm.

(15) 2, 2 -Methylenebis - (3, 4, 6-trichlorophenol): fungistat: industrial uses, finishing process. [Ref. I-M-13-00.03]

(a) -200 to 2500 ppm.

(b) 2500 to 6000 ppm plus 2500 to 6000 ppm o-phenylphenol.

(16) 10, 10 - Oxybisphenoxarsine: fungistat: industrial uses in finishing process. [Ref. I-O-03-00.01] For cotton fabrics to be coated with thermoplastic systems: 400 to 1000 ppm by padding.

(17) Pentachlorophenol: consumer use. 30,000 to 50,000 ppm as a soak. [Ref. I-P-05-00.01]

(18) Sodium dimethyldithiocarbamate: fungistat: industrial uses in finishing process. [Ref. I-S-09-00.05] 1.38% plus 0.12% sodium 2-mercaptobenzothiazole by padding to 100% wet pick up. Set with zinc acetate.

(19) Sodium pentachlorophenate: fungistat: industrial use in finishing process. [Ref. I-S-15-00.04] For suit linings, upholstery fabrics: 1000 to 5000 ppm by dipping, padding or spraying.

(20) Sodium orthophenylphenate: fungistat for preservation of unfinished cloth and yarns. [Ref. I-S-16-00.10] 0.2 to 1.0%.

(21) Sodium salt of 2-mercaptobenzothiazole: fungistat; industrial use in finishing process. [Ref. I-S-20-00.01] 0.2% by weight deposited on fabric.

(22) Thiram: fungistat: industrial uses. [Ref. I-T-10-00.08] For belting, ducks, other heavy industrial fabrics: 1875 to 3750 ppm by weight of fabric.

(23) 3, 4', 5-Tribromosalicylanilide: fungistat: industrial use in finishing process. [Ref. I-T-11-00.01 and 0.2]

(a) For fabrics to be coated with vinyl thermoplastics: 20,000 ppm prior to coating.

(b) Other textiles: 500 to 7500 ppm by weight.

(24) Tributyltin acetate: fungistat: industrial use in finishing process. [Ref. I-T-12-00.01] Deposit 1.8% of product by weight of fabric by padding.

(25) Zinc dehydroabietylammonium 2-ethylhexoate: fungistat: industrial use in finishing process. [Ref. I-2-03-00.01] 2.0 to 2.5% or more by weight of fabric of a formulation containing 42.8% plus 29.2% zinc ethylhexoate and 19.2% 2-ethylhexoate salt of magnesium quinolinolate.

### C. Comparative effectiveness and impact.

(1) Various mercury compounds are used as fungistats in textile finishing at levels of 25 to 1130 ppm by impregnation. Substitute materials are used at levels from 200 to 20,000 ppm.

(2) Mercury compounds are "broad spectrum" fungistats controlling most, if not

all, of the problem organisms. Substitute materials are less broad and frequently require combinations of materials to aid effectiveness.

(3) Mercury compounds are useful on a broad range of fabric and textile substrates (cotton, jute, wool, etc.). Substitute materials are adapted to more specific uses.

(4) Mercury compounds are less expensive than substitute materials, frequently by a factor of 10.

(5) Mercury compounds do not impart objectionable coloration nor do they affect the "hand" of textiles as do many substitute compounds.

(6) Impact of withdrawal of mercury for use on fabrics and textiles may affect financial situation of certain economic poison formulators and may require revision of certain Federal specifications. Impact on consumer of treated goods should be slight to moderate.

## 2. Bacteriostats

### A. Mercury compounds

(1) Phenylmercuric borate: (1.1%) and alkyl (40% $C_{12}$, 50% $C_{14}$, 10% $C_{16}$) dimethyl benzyl ammonium chloride (0.12%) and Phenylmercuric chloride (0.10%): [Ref. 3673-10] Add 2 lb product to 100 gal of finishing bath; for cotton, wool, nylon and rayon fibers.

(2) Pyridyl mercuric acetate (2%) and alkyl (67% $C_{12}$, 25% $C_{14}$, 7% $C_{16}$, 1% $C_8$-$C_{18}$) dimethylbenzyl ammonium chorides (7.5%): [Ref. 5817-2]
2% solution of product at 100°F, 60-65% wet pickup by fabric resulting in 1.2 to 1.3% of product on fabric (types not specified)

(3) Phenylmercuric triethanolammonium lactate (22.5%): [Ref. 6516-4] Typical formula: 3.75 lb product to makeup 100 gal of water. Padding application from aqueous solution sufficient to deposit 0.25% of product manufactured dry weight of fabric (unspecified).

### B. Substitute compounds

(1) Bis (tributyltin) oxide (0.84%) and dialkyl (alkyl from coconut oil fatty acids) dimethyl ammonium chloride (1.25%): [Ref. 10466-2] 1.25% product on weight of goods.

(2) Alkyl (average = $C_{12}$) amine salts of tetrachlorophenol (100%): [Ref. 3090-46] 0.25% to 2% product based on weight of dry fabric.

(3) Bis (tri-n-butyltin) oxide (25%): [Ref. 6390-2] 0.1 to 0.2% product based on dry weight of fabric.

(4) n-alkyl (60% $C_{14}$, 30% $C_{16}$, 5% $C_{12}$, 5% $C_{18}$) dimethyl benzyl ammonium choride (50%): [Ref. 6390-9] Apply to leave 0.25% product on dry weight of fabric.

(5) n-alkyl (60% $C_{14}$, 30% $C_{16}$, 5% $C_{12}$, 5% $C_{18}$) dimethyl benzyl ammonium 2 ethyl hexoate (25%): [Ref. 6390-13] 0.1% pickup or 0.025% active ingredient on dry weight of fabric.

(6) Tributyltin neodecanoate (98%). [Ref. 8314-5] 0.025% to 0.05% product based on weight of fabric.

(7) Zinc dimethyldithiocarbamate (46%) and zinc mercaptobenzothiazole (4%): [Ref. 1965-26] 2.5% product by weight of cloth.

(8) Sodium pentachlorophenate (79%) [Ref. 464-125] 0.1% to 0.75% by weight of treated material.

(9) 2, 2 -methylenebis (4-chlorophenol): [Ref. 824-6] 40% solution used to deposit 0.5% to 1.0% on fabric, concentration of product in pad liquor varies with percent pickup.

### C. Comparative effectiveness and impact

(1) Substitute compounds exhibit greater substantivity to fabrics than mercurials.

(2) Substitute compounds appear to be satisfactory.

(3) Impact on certaiin individual firms selling mercurials may be substantial, impact on industry and consumer expected to be minimal.

## III. Fibers and Cordage

### 1. **Fungistats**

### A. **Mercury compounds**

(1) Phenylmercuric acetate: [Ref. I-P-08-00.10] For interior components of furniture and mattresses (alpha cellulose, cotton, latex impregnated curled hair, sisal, etc.) - fungistat: 150 to 300 ppm by spraying.

(2) Phenylmercuric borate and phenylmercuric chloride plus alkyl dimethyl benzyl ammonium chloride: [Ref. I-A-08-45.05] For cotton, wool, and synthetic fibers - fungistat: 0.22 lb of PMB plus 0.020 lb of PMC plus quaternary/100 gal by dip, spray, or brush (264 ppm PMB plus 24 ppm PMC).

(3) Phenylmercuric oleate plus zinc naphthenate: [Reg. No. 2553-6 and I-P-14-00.01] For rope, twine.

(a) Household use: dip cordage to saturate fibers in 2.5% PMO plus 12.5% zinc naphthenate.

(b) Household use: dip cordage to saturate all fibers in 0.6% PMO plus 7.125% pentachlorophenol.

(c) Industrial use: animal, vegetable and synthetic filling material for furniture, mattresses, pillows: spray with 10 parts of 30% PMO in 90 parts of spray oil and water (30,000 ppm PMO).

### B. **Substitute compounds**

(1) Alkyl dimethyl benzyl ammonium chlorides: [Ref. I-A-08-45.02, Reg. No. 3533-29] Air conditioning filters: 1000 ppm or 2.8% mixture of quaternary, sodium dimethyl-dithiocarbonate and sodium 2-mercaptobenzothiazole.

(2) Copper naphthenate - cordage: [Ref. I-C-30-00.01] 1.0 to 2.0% metallic copper equivalent.

(3) Copper 8-quinolinolate - cordage: [Ref. I-C-34-00.01] To retain 1.0% or more actual.

(4) Creosote - cordage: [Ref. I-C-41-00.01] 40 to 100% dip.

(5) Dialkyl dimethyl ammonium chloride: [Ref. I-D-04-20.01]

(a) Air conditioning filters: Deposit 1432 ppm quaternary plus 285 ppm benzoic acid and 263 ppm salicylic acid by dip, spray, or sponge.

(b) For interior components of furniture and mattresses: 1.3 lb quaternary plus 0.26% TBTO by spraying; or 0.0375 lb quaternary plus 0.05% TBTO in dye - beck or padder; or 0.025% quaternary plus 0.008% TBTO for cotton batting only.

(6) Lauryl pyridinium salt of 5-chloro-2-mercaptobenzothiazole: [Ref. I-L-01-00.01] Industrial use in finishing process:

(a) Burlap: 3,375 to 10,000 ppm.

(b) Duck, mattress ticking, similar fabrics: 1200 to 2500 ppm.

(c) Industrial fabrics to yarns: 5,000 to 10,000 ppm.

(7) Pentachlorophenol - cordage: [Ref. I-P-05-00.01] 3.0 to 5.0% by dipping.

(8) Sodium - o-phenylphenate: [Ref. I-S-16-00.08] Air filters: spray using 0. % SOPP plus 0.2% sodium propionate and 0.2% 2, 2-methylenebis ( 3, 4, 6-trichlorophenol)

(9) Zinc dehydroabietylammonium 2-ethylhexoate - cordage: [Ref. I-Z-03-00.01] Use 2.5 to 5.0% or more by weight.

(10) Zinc naphthenate - cordage: [Ref. I-Z-05-00.01] Use 1.8 to 5.0% product as a dip.

### C. **Comparative effectiveness and impact**

(1) Several substitute materials are available for use on air conditioning filter fibers and interior components of furniture and mattresses.

(2) The impact of withdrawal of mercury on fibers and cordage would appear to be slight on industry and insignificant on the consumer.

### 2. **Bacteriostats**

### A. **Mercury compounds**

(1) Phenylmercuric acetate (30%): [Ref. 3090-127] 1 lb product per 3333 lb ma-

terial, or 0.03% product based on finished weight of material; apply as spray.

(2) Phenylmercuric acetate (15%): [Ref. 3090-28] 10 parts product to 90 parts water; spray on material depositing 0.3% of total mixture in the filling material.

### B. Substitute compounds

(1) Bis (tri-n-butyltin) oxide (25%): [Ref. 6390-7] 0.1 to 0.2% by weight of material.

(2) n-Alkyl (60% $C_{14}$, 30% $C_{16}$, 5% $C_{12}$, 5% $C_{18}$) dimethylbenzyl ammonium chloride (50%): [Ref. 6390-9] Apply to leave 0.25 to 1% product by weight.

(3) n-Alkyl (60% $C_{14}$, 30% $C_{16}$, 5% $C_{12}$, 5% $C_{18}$) dimethyl benzyl ammonium 2 ethylhexoate (25%): [Ref. 6390-13] Apply to yield 0.025% active ingredient by weight.

(4) Tributyltin neodecanoate (98%): [Ref. 8314-5] 0.1 to 2% product by weight of material.

(5) Alkyl (average $C_{12}$) amine salts of tetrachlorophenol (100%): [Ref. 3090-146] 0.25 to 2% product based on dry weight of material.

(6) Sodium pentachlorophenate (79%) and sodium salts of other cholorophenols (11%): [Ref. 464-125] 0.1 to 0.75% product by weight of material treated.

(7) Zinc dimethyldithiocarbamate (46%) and zinc 2-mercaptobenzothiazole (4%): [Ref. 1965-26] 1 to 1.5% product by weight of material.

(8) Sodium pentachlorophenate (79%): [Ref. 464-125] 0.1 to 0.75% product by weight of treated material.

### C. Comparative effectiveness and impact

(1) Substitute compounds appear to be adequate.

(2) Impact on industry and consumer expected to be minimal.

## IV. Food, Feed and Tobacco Crops (see also XI, Seed Treatments)

### 1. Cotton

### A. Mercury compounds

Cyano (methylmercuric) guanidine: [Ref. I-C-46-00.01] 0.016 lb plus 0.68 to 0.72 lb of pentachloronitrobenzene/acre (12,400 linear ft of row) in furrow and covering soil at time of planting. For soil-borne seedling diseases.

### B. Substitute compounds

(1) Captan: [Ref. I-C-10-00.11] 4 to 6 lb/acre (12,400 linear ft of row) or 1.0 lb plus 1.0 lb pentachloronitrobenzene/12,400 linear ft of row in furrow and covering soil at time of planting.

(2) Chloroneb: [Ref I-C-16-00.11] 1.0 to 2.0 lb/12,400 linear ft of row

(3) Dichlone: [Ref. I-D-06-00.04] 0.5 lb/12,400 linear ft of row.

(4) 5-Ethoxy-3-trichloromethyl-1, 2, 4-thiadiazole: [Ref. I-E-01-00.01] 0.25 to 0.37 lb plus 1.0 to 1.5 lb of pentachloronitrobenzene/12,400 linear ft or row.

(5) Monosodium salt of 2, 2-Methylenebis- (3, 4, 6-trichlorophenol): [Ref. I-M-22-00.01] 0.560 to 1.125 oz/12,400 linear ft of row.

(6) Pentachloronitrobenzene: [Ref. I-P-04-00.06] 1.0 to 5.0 lb/12,400 linear ft of row.

(7) Zinc ion- maneb coordination product: [Ref. I-Z-04-00.06]

(a) 0.45 to 1.2 lb/12,400 linear ft of row.

(b) 0.3 lb plus 0.3 lb PCNB/12,400 linear ft of row.

(8) Zineb: [Ref. I-Z-10-00.08]

(a) 2.25 to 3.75 lb/12,400 linear ft of row.

(b) 1.3 lb plus 0.75 lb captan and 1.15 lb PCNB/12,400 linear ft of row.

### C. Comparative effectiveness and impact

(1) Mercury is a highly effective fungicide at very low dosage rates, and the spectrum of organisms it controls is broadened by formulating with PCNB.

(2) Substitute compounds must be used at dosages from 30 to almost 400 times more than mercury.

(3) The cost of using substitute materials is 50 to 1000 times the cost of mercury.

(4) Substitute compounds are sometimes as effective as mercury when used as directed for this purpose.

(5) The impact of withdrawal of mercury for this use will be very slight on industry but will add to the farm cost of growing cotton.

## 2. Tobacco

### A. Mercury compounds

Hydroxymercurichlorophenol: [Ref. I-H-06-00.01] For seed beds only, where plants are withdrawn and transplanted: 0.0143 to 0.0214 lb/10 sq ft (9.15 lb/acre). For damping-off control.

### B. Substitute compounds

(1) Chloranil (shade tobacco only): [Ref. I-C-12-00.03] 0.5 lb/25 gal as a drench.

(2) Formaldehyde: [Ref. I-F-03-00.02] 1 gal of 8000 ppm solution.

(3) Methyl bromide: [Ref. I-M-06-00.02] 1 to 2 lb/100 sq ft with tarpaulin, or 20 to 50 gal of 69.0% formulation/acre by chisel method.

(4) Tetrahydro-3, 5-dimethyl-2H, 1, 3, 5-thiadiazine- 2-thione (Mylone): [Ref. I-T-07-00.01] 4.1 lb/80 to 100 sq yd.

### C. Comparative effectiveness and impact

(1) Substitute materials are about as effective as mercury.

(2) Mercury is much less expensive to purchase and apply, but substitute chemicals also control other diseases at the same time.

(3) Mercury has not been used extensively for this purpose in recent years, and the impact on manufacturer and consumer of withdrawal of mercury for this use will be negligible. Note: The manufacturer of this mercury product has stated that it is being withdrawn from production. Registration has continued to cover stocks still in dealers hands.

## 3. Farm and Greenhouse Equipment

### A. Mercury compounds

Cyano (methylmercuric) guanidine: [Ref. I-C-46-00.03] For farm machinery, greenhouse benches, empty flats, pots, tools and walks. Plant pathogen disinfection. 1.7 ppm spray or dip. No food contamination.

### B. Substitute compounds

Alkyl dimethyl benzyl ammonium chlorides. [Ref. I-A-08-05.01 and I-A-08-50.01] 1800 to 5900 ppm.

### C. Comparative effectiveness and impact

(1) Mercury compounds are far more effective than substitute materials for this use and at very low dosage rates.

(2) Impact of withdrawal of mercury for this use will be severe on nurserymen and potato growers; slight on manufacturers.

## V. Food and Feed Containers (Sacks, Seed Bins, and Containers for Treated Seed Subject to Diversion to Food and Feed Uses)

### 1. Mercury compounds

Hydroxymercurichlorophenol: [Ref. I-H-06-00.05] 690 ppm suspension. Spray or dip before refilling. Fungistat.

### 2. Substitute compounds

None registered.

### 3. Comparative effectiveness and impact

a. Several substitute materials could be accepted for this use, particularly the non-residual disinfectants such as the hypochlorites. Quaternary compounds, TBTO, etc. would require tolerances for use on seed which could be diverted to food or feed uses. Copper naphthenate and zinc petroleum sulfonate can also be used.

B. Impact of withdrawal of this use for mercury would be negligible. Note: The manufacturer has indicated that the product is being discontinued. Registration remains in effect to cover stocks still on distributors shelves.

## VI. Humans

### 1. Mercury compounds

A. Metallic mercury: [Ref. Reg. Nos.: 140-20; 223-12; 372-19; 1091-5; 1471-3; 5231-3; 6253-3; 9850-1] 9.0 or 10% mercury for louse control applied as an ointment.

B. Ammoniated mercury: 5.0% [Ref. Reg. Nos. 994-5] (3.9% metallic mercury) for louse control applied as an ointment.

C. Metallic mercury: (10%) plus Mercury oleate (0.8%) [Ref. Reg. No. 4476-30; 6253-3] For louse control applied as an ointment.

### 2. Substitute compounds

A. Premium grade Malathion: 1% dust for head and body lice [Ref. Reg. No. 241-68] (Basic manufacturer of malathion does not market for this purpose).

B. Carbaryl (Sevin): 5% dust for crab, head and body lice [Ref. Reg. No. 9734-3]

C. Lindane: 1% dust is registered for use by the military or under prescription from a physician.

D. Thanite: 5% water emulsion [Ref. Reg. No. 718-1]

E. Products containing pyrethrins, sabadilla, and larkspur have also been registered for control of lice on humans; however, we can not identify any products which are currently being marketed for this purpose.

F. DDT has been registered for control of lice on humans; however, all uses of DDT have been cancelled, and administrative hearings are to take place in the near future.

### 3. Comparative effectiveness and impact

The primary problems with products used against lice are in two areas:

(1) resistance in certain parts of the world has developed to one or more of the chemicals registered for control of lice;

(2) Malathion and certain of the other compounds are not readily available to the general public.

## VII. Ornamental Plants

### 1. Bulbs and Corms

#### A. Mercury compounds

(1) Cyano (methylmercuric) guanidine: [Ref. I-C-46-00] For root, stem and bulb rots: 5.0 ppm solution. Soak.

(2) Mercurous chloride: (alone or with mercuric chloride) [Ref. I-M-0500.01] Gladiolus corms only. 0.9 [illegible] gal. Dip.

(3) N-Methylmercuri-1, 2, 3, 6-tetrahydro-3, 6-endomethano-3, 4, 5, 6, 7, 7-tetrachlorophthalimide: [Ref. I-M-15-00.01] Gladiolus corms only: 1 pt of 10.0% formulation/50 gal. Soak.

(4) Phenylmercuric acetate: [Ref. I-P-08-00.03] Bulbs: 2.0 fl. oz of 10% formulation/2 gal. Soil soak.

(5) Phenylmercuric triethanol ammonium lactate: [Ref. I-P-17-00.02] 117 to 750 ppm dip.

(6) Sodium ethylmercuri thiosalicylate: [Ref. I-S-11-00.01] For bulbs and corms: 2 to 3 pt of 12% solution/100 gal. Soak.

#### B. Substitute compounds

(1) Copper chloride: [Ref. I-C-26-50.01] Household use: For Fusarium rot only - 1 tbs/gal/12 sq ft of soil. Minimal effectiveness.

(2) p-(Dimethylamino) benzenediazo sodium sulfonate: [Ref. I-D-14-00.02] 1.25 to 2.8 oz/50 gal/400 sq ft, or use 0.5 pt above solution/each 6-inch pot.

(3) Methyl isothiocyanate: [Ref. I-M-07-00.01] 25 to 50 gal/acre.

(4) Sodium o-phenylphenate: [Ref. I-S-16-00.07] Bulbs, Corms - rots: 514 ppm. solution as tetrahydrate. Soak.

(5) 2-(4-thiazolyl) benzimidazole (Thiabendazole): [Ref. I-T-09-00.01]: Bulbs, Corms-Fusarium rot: 1080 ppm. Soak.

(6) Thiram: [Ref. I-T-10-00.08] Bulbs, Corms- decays. Dust with 4.0 to 12.0% formulation.

#### C. Comparative effectiveness and impact

(1) Effectiveness of substitute compounds ranges from low to comparable to mercury compounds.

(2) Impact of withdrawal of mercury for these uses will be slight on manufacturer but much more costly to florist and nurseryman.

### 2. Cuttings

#### A. Mercury compounds

(1) Cyano (methylmercuric) guanidine: [Ref. I-C-46-00.02] 2.5 ppm solution. Dip. Soil-borne diseases.

(2) Methylmercury hydroxide: [Ref. I-M-18-00.01] Carnation cuttings only: 2.2 ppm. Dip.

#### B. Substitute compounds

(1) 8-Quinolinol benzoate: [Ref. I-Q-01-00.01] 250 to 500 ppm solution. Soak soil. Damping-off.

(2) 8-Quinolinol sulfate: [Ref. I-Q-03-00.01] 180 to 260 ppm solution. Dip cuttings or soak soil. Soil-borne diseases.

(3) Thiram: [Ref. I-T-10-00.04] 15,000 ppm dust as dip for hardwoods, or 3 oz of 15% formulation/pt as softwood dip.

#### C. Comparative effectiveness and impact

(1) Mercury is more effective than the substitute compounds against a broader range of pathogens and at lower dosages and lower costs.

(2) Other, now unregistered products, are available or will soon be available with good effectiveness for these uses but at much higher cost.

(3) The impact of withdrawal of mercury for treating cuttings will be negligible on the manufacturer but severe on the nursery-

man or florist until suitable inexpensive replacements are available.

### 3. Flowering and Foliage Plants (Soil treatments)

#### A. Mercury compounds

(1) Cyano (methylmercuric) guanidine [Ref. I-C-46-00.02] 2.5 to 5.3 ppm as soil drench for soil-borne diseases.

(2) Hydroxymercurichlorophenol: [Ref. I-H-06-00.01] 0.0143 to 0.0214 lb/10 sq ft.

(3) Phenylmercuric acetate: [Ref. I-P-08-00.04] 26 ppm solution as soil spray.

#### B. Substitute compounds

(1) Captan: [Ref. I-C-10-00.12] 15 gal of 1200 ppm solution/1000 sq ft.

(2) Chloropicrin: [Ref. I-C-19-00.01]

(a) 485 to 1976 lb/acre with cultipack or water seal.

(b) 150 to 200 lb/acre with plastic seal.

(c) 82 to 115 lb plus 168 to 235 lb methyl bromide/acre with plastic seal.

(d) 319 lb plus 240 lb Dichloropropenes/acre with plastic seal.

(3) p-(Dimethylamino) benzenediazo sodium sulfonate: [Ref. I-D-14-00.02]: 1.25 to 2.8 oz/50 gal/400 sq ft or 1 pt above solution/each 6-inch pot.

(4) Methyl bromide: [Ref. I-M-06-00.02] 1 to 2 lb/100 sq ft with tarpaulin. 20 to 50 gal of 65% formulation/acre by chisel application.

(5) Methyl isothiocyanate: [Ref. I-M-07-00.01] 25 to 50 gal/acre

(6) Pentachloronitrobenzene: [Ref. I-P-04-00.07] 27 to 232 lb/100 gal or 65 to 232 lb as a dust/acre.

(7) Tetrahydro-3, 5-dimethyl-2H-1, 3, 5: thiadiazine-2-thione (Mylone): [Ref. I-T-07-00.02]: 4.1 lb/10 to 80 sq yd.

#### C. Comparative effectiveness and impact

(1) Highly effective substitute compounds are already registered for this use and are widely employed.

(2) Impact of withdrawal will be slight on manufacturers and consumers alike.

### 4. Flowering and Foliage Plants (Foliar treatments)

#### A. Mercury compounds

(1) Cyano (methylmercuric) guanidine: [Ref. I-C-46-00.02] 25 ppm. Apply as necessary.

(2) Phenylmercuric triethanol ammonium lactate: [Ref. I-P-17-00.01] Gladiolus only. 146 ppm. Dip flower spikes before shipment or storage. Laurel and Rhododendron: 94 ppm in 2 or 3 applications.

#### B. Substitute compounds

(1) Benomyl: [Ref. I-B-02-00.02] 4 oz/100 gal, as required.

(2) Captan: [Ref. I-C-10-00.11 through .13] 1.0 lb/100 gal or 2.1 lb as a dust/acre, as required.

(3) Copper-Bordeaux: [Ref. I-C-25-00.08] Use 2-2-50 to 4-4-50 mixtures as required.

(4) Copper oleate: [Ref. I-C-30-50.03] Up to 4 lb of 25% formulation/gal. Homeowner use, as required.

(5) Copper oxychloride: [Ref. I-C-32-00.06 and .07] 2.1 lb metallic copper equivalent/100 gal; 0.125 to 0.25 oz of metallic copper plus 0.1 to 0.2 oz of sulfur and 0.025 to 0.050 oz of zineb/gal. Household use, as required.

(6) Copper oxychloride sulfate: [Ref. I-C-33-00.08] 1.25 to 2.2 lb metallic copper equivalent/100 gal, or 1.4 to 3.5 lb as a dust/acre. As required.

(7) Copper 8-quinolinolate: [Ref. I-C-34-00.01] 1.0 oz of 2.0% formulation plus Karathane (dinocap) and petroleum distil-

late/3000 cu ft of greenhouse space, as required.

(8) Copper sulfate, basic: [Ref. I-C-36-00.09] 2.0 lb metallic copper equivalent/100 gal. As required.

(9) Copper dihydrazinium sulfate: [Ref. I-C-28-00.01] 3000 to 4000 ppm solution, as necessary. Roses only.

(10) Copper oleate: [Ref. I-C-30-50.03] Up to 4 tbs./gal as necessary. Homeowner use.

(11) Copper oxychloride: [Ref. I-C-32-00.06] 2.12 lb as metallic copper equivalent/100 gal (2545 ppm) as necessary.

(12) Copper oxychloride sulfate, basic: [Ref. I-C-33-00.07 and .08] 1.2 to 2.2 lb as metallic copper equivalent/100 gal (2640 to 6940 ppm) as necessary.

(13) Copper sulfate, basic: [Ref. I-C-36-00.09 and .10] 3.0 to 3.18 lb metallic copper equivalent/100 gal (approx. 3600 ppm) as necessary.

(14) Copper-Zinc-Chromate Complex: [Ref. I-C-40-00.03 and .04] 1.8 lb actual/100 gal or 1.7 to 2.3 lb/acre dust.

(15) 2, 6-Dichloro-4-nitroaniline: [Ref. I-D-09-00.06] 0.28 to 0.56 lb/100 gal or 0.64 to 1.8 lb as a dust/acre at 5- to 14-day intervals.

(16) Cycloheximide: [Ref. I-D-16-00.01] 2.0 ppm solution at 3- to 7-day intervals.

(17) Ferbam: [Ref. I-F-01-00.08 and .09] 0.76 to 1.14 lb/100 gal or dust to cover at 7- to 10-day intervals

(18) Folpet: [Ref. I-F-02-00.05 and .06] 0.5 to 1.0 lb/100 gal (600 to 1200 ppm)

(19) Glyodin: [Ref. I-G-02-00.02] 200 to 480 ppm solution as required.

(20) Maneb: [Ref. I-M-02-00.09 and .10] 0.8 to 1.2 lb/100 gal (1000 to 1500 ppm) or 1.2 to 2.4 lb dust/acre.

(21) Karathane (dinocap): [Ref. I-M-14-00.04] 1.5 to 3.84 lb/100 gal as necessary.

(22) 3 (2-methylpiperidino) propyl 3, 4-dichlorobenzoate: [Ref. I-M-26-00.01] 0.25 to 0.5 lb/100 gal (300 to 600 ppm) at 7-day intervals.

(23) Nabam: [Ref. I-N-01-00.08] o.43 to 0.86 lb/100 gal at 7-day intervals.

(24) Potassium polysulfide: [Ref. I-P-27-00.01] 3 fl oz of 2.9% solution/100 gal at 7- to 10-day intervals.

(25) 8-Quinolinol sulfate: [Ref. I-Q-03-00.01] 180 to 390 ppm solution at 7-day intervals.

(26) Sodium o-phenylphenate: [Ref. I-S-16-00.07] 514 to 1030 ppm at 7- to 14-day intervals.

(27) Streptomycin: [Ref. I-S-23-00.03] 50 to 200 ppm at 3- to 7-day intervals.

(28) Sulfur: [Ref. I-S-24-00.09 through .11] 4.75 to 5.6 lb/100 gal or dust to cover at 5- to 10-day intervals.

(29) 1, 2, 4, 5-Tetrachloro-3-nitrobenzene: [Ref. I-T-03-00.01] 1 oz/10,000 cu ft of greenhouse space by vaporization.

(30) Tetrachloroisophthalonitrile: [Ref. I-T-05-00.01] 0.75 to 1.126 lb/100 gal or 8.0 gm/4000 cu ft of greenhouse space by vaporization.

(31) Thiram: [Ref. I-T-10-00.03 through .05] 0.65 lb/100 gal or 5.0 to 12.0% dusts.

(32) Zinc ion-maneb complex: [Ref. I-Z-04-00.07 through .09] 1.2 lb/100 gal at 7- to 10-day intervals.

(33) Zineb: [Ref. I-Z-10-00.09] 1.125 to 1.5 lb/100 gal as required

(34) Ziram: [Ref. I-Z-11-00.05 and .06] 1.14 to 6.3 lb/100 gal at 7- to 10-day intervals.

### C. Comparative effectiveness and impact

(1) Most substitute compounds are more effective than mercury compounds against the foliar diseases of flowering and foliage plants.

(2) Impact of withdrawal of mercury compounds for such uses will be insignificant on manufacturer and consumer.

### 5. Trees and Shrubs (Foliar application for disease control)

#### A. Mercury compounds

(1) Methylmercury 8-hydroxyquinolinolate: [Ref. I-M-19-00.01 and .02] For anthracnose, leaf blights, leaf spots, twig blights. 1 oz/100 gal (75 ppm solution). Spray.

(2) Phenylmercuric acetate: [Ref. I-P-08-00] For anthracnose, leaf blight, leaf spots, twig blights. 125 ppm solution, spray.

(3) Phenylmercuric dimethyldithiocarbamate: [Ref. I-P-] For twig blight on eastern red cedar only, in nurseries. 180 ppm solution, spray at 10- to 14-day intervals.

(4) Phenylmercuric triethanol ammonium lactate: [Ref. I-P-]

(a) For elm leaf spot only: 9.4 ppm spray at 2- to 3-week intervals.

(b) For hickory, maple, oak, etc. anthracnose, leaf spots. Use 9.4 to 19.0 ppm spray as required.

#### B. Substitute compounds

None directing use on trees specified for mercury compounds. Maneb is used for anthracnose on dogwood and might be somewhat effective on other trees.

#### C. Comparative effectiveness and impact

(1) Adequate substitutes for mercury are not registered.

(2) Impact of withdrawal of mercury compounds for these uses would be slight on the manufacturer but severe on the consumer and would result in loss of many trees, particularly Sycamore severely injured by anthracnose. Cost of tree removal on city streets and in parks is very high.

### 6. Trees and Shrubs (Injection application)

#### A. Mercury compounds

Mercuric chloride: [Ref. I-M-04-00.02] For Dutch Elm disease. Inject 0.12% solution in methyl alcohol.

#### B. Substitute compounds

None

#### C. Comparative effectiveness and impact

Impact of withdrawal of mercury for this will be highly important to the manufacturer, but product is of doubtful or marginal value, and impact on disease control will be very slight to negligible.

### 7. Trees and Shrubs (wound dressings)

#### A. Mercury compounds

(1) Mercuric chloride: [Ref. I-M-04-00.02] 1930 ppm.

(2) Phenylmercuric nitrate: [Ref. I-P-13-00.01] 3000 ppm.

#### B. Substitute compounds

(1) Copper naphthenate: [Ref. I-C-30-00.01] 3.3 to 10.0% in asphalt.

(2) Copper sulfate, basic: [Ref. I-C-36-00.10] 1.9% as metallic copper equivalent plus 1.2% phenol.

(3) Sodium o-phenylphenate: [Ref. I-S-16-00.07] 2.0% tetrahydrate paste.

(4) Thiram: [Ref. I-T-10-00.05] 1.0% paste or in asphalt.

#### C. Comparative effectiveness and impact

(1) Effectiveness of substitute compounds is probably about equal to that of mercury.

(2) Impact on withdrawal of mercury for this use would be neglibible.

## VII. 8. Turf Disease Control

| Compounds | Brown patch | Copper spot | Damping-off | Dollar spot | Helminthosporium complex | Pink patch or Red thread | Pythium | Snow molds |
|---|---|---|---|---|---|---|---|---|
| | ounces actual per 1000 square feet | | | | | | | |
| A. **Mercury compounds:**<br>(1) Cyano (methyl-mercuric) guanidine [Ref. I-C-46-00.02] | .033 | .033 | .066 | .033 | .066 | | | .066 |
| (2) Hydroxymercuric - chlorophenol: [Ref. I-M-06-00.01] | .823 | .300 | | .823 | .300 | .300 | | .800 |
| (3) Mercuric chloride [Ref. I-M-04-00.01] | 1 – 3 | | | | | | | 4 |
| (4) Mercuric chloride plus Mercurous chloride [Ref. I-M-04-00.01] | .3 – .9<br>+<br>.6 – 2.4 | | | .3 – .9<br>+<br>.6 – 2.4 | | | | |
| (5) Mercuric dimethyl - dithiocarbamate [Ref. I-M-04-05.01] | .444 | .444 | | .444 | .444 | .444 | | |
| (6) Methylmercuri tetrahydroendo - methano hexachloro - phthalimide [Ref. I-M-15-00.01] | .1 | .1 | | .1 | .1 | | .2 | |
| (7) Mercurous chloride [Ref. I-M-05-00.01] | .9 – 1.5 | | | .9 – 1.8 | | | | |
| (8) Phenylmercuric acetate [Ref. I-P-08-00.04] | .1 | .1 | .1 | .1 | .1 | .1 | .1 | .1 – .2 |
| (9) Phenylmercuric dimethyldithio-carbamate [Ref. I-P-09-00.01] | .1 – .2 | .1 – .2 | | .1 – .2 | | | | |

### VII. 8. Turf Disease Control–Continued

| Compounds | Brown patch | Copper spot | Dumping-off | Dollar spot | Helminthosporium complex | Pink patch or Red thread | Pythium | Snow molds |
|---|---|---|---|---|---|---|---|---|
| | ounces actual per 1000 square feet | | | | | | | |
| (10) **Phenylmercuric monoethanol ammonium lactate** [Ref. I-P-12-00.01] | .13 | .13 | | .13 | .13 | .13 | | .13 to .26 |
| (11) **Phenylmercuric triethanol ammonium lactate** [Ref. I-P-17-00.01] | .15 | .15 | | .15 | .15 | .15 | | .15 to .20 |
| **B. Substitute compounds:** | | | | | | | | |
| (1) Benomyl [Ref. I-B-02-00.02] | .5 – 1 | | | .5 – 1 | | | | .5 – 1 |
| (2) Cadmium-calcium-copper-zinc-chromate complex [Ref. I-C-01-00.01] | 3 – 4 | 3 – 4 | 3 | 3 – 4 | | 3 – 4* | | 8 – 12 |
| (3) Cadmium carbonate [Ref. I-C-02-00.01 | | .23 | | .23 | | .23* | | |
| (4) Cadmium chloride [Ref. I-C-03-00.01] | .2 | .2 | .2 | .2 | .2 | .2* | | .2 – .4 |
| (5) Cadmium sebacate [Ref. I-C-04-00.01] | .1 – .4 | .1 – .4 | | | .1 – .4 | .1 – .4* | | |
| (6) Cadmium succinate [Ref. I-C-05-00.01] | | .3 | | .3 | | .3* | | 1.2 to 2.4 |
| (7) Captan [Ref. I-C-10-00.12] | 16 – 32 | 16 – 32 | 16 – 32 | | 16 – 32 | | | |
| (8) Chloranil [Ref. I-C-12-00.03] | 3.2 | | | | | | | |

## VII. 8. Turf Disease Control–Continued

| Compounds | Brown patch | Copper spot | Damping-off | Dollar spot | Helminthosporium complex | Pink patch or Red thread | Pythium | Snow molds |
|---|---|---|---|---|---|---|---|---|
| | ounces actual per 1000 square feet | | | | | | | |
| (9) Chloroneb [Ref. I-C-12-00.02] | | | | | | | 2.6 | 3.9 to 5.9 |
| (10) Copper-zinc-chromate complex [Ref. I-C-40-00.04] | 1 gal. of .1 – .33 % soln. | | | | | | | 1 gal. of .1 – .3 % soln. |
| (11) Crystal violet-auramine-malachite green [Ref. I-C-45-00.01] | .5 | | | | | | | |
| (12) 2, 4-Dichloro-6-(o-chloroanilino)-s-triazine (Dyrene) [Ref. I-D-07-00.03] | 2 to 4 | 2 to 4 | | 2 to 4 | 2 to 4 | | | 2 |
| (13) p-(Dimethylamino) benezenediazo sodium sulfonate [Ref. I-D-14-00.02] | | | | | | | 1.4 to 1.8 | |
| (14) Cycloheximide [Ref. I-D-16-00.01] | .318 | | | | .318 | | | |
| (15) Folpet [Ref. I-P-02-00.06] | | | | | 3 | | | |
| (16) Maneb [Ref. I-M-02-00.10] | 2.4 to 6.4 | | | 4.8 to 6.4 | 2.4 to 6.4 | | | |
| (17) Pentachloronitro-benzene [Ref. I-P-04-00.08] | 2.15 to 78.4 | | | 78.4 to 158.4 | | | | 16.0 to 78.4 |
| (18) Chlorophthalonil [Ref. I-T-05-00.02] | 1.5 to 6.0 | | | 1.5 to 3.0 | 1.5 to 6.0 | | | 4.5 to 6.0 |

## VII. 8. Turf Disease Control–Continued

| Compounds | Brown patch | Copper spot | Damping-off | Dollar spot | Helminthosporium complex | Pink patch or Red thread | Pythium | Snow molds |
|---|---|---|---|---|---|---|---|---|
| | ounces actual per 1000 square feet | | | | | | | |
| (19) 2-(4-Thiazolyl) benzimidazole [Ref. I-T-09-00.02] | .6 – 1.2 | | | .6 – 1.2 | | | | .6 – 1.2 |
| (20) Thiram [Ref. I-T-10-00.04] | 1.9 to 4.5 | 2.0 to 3.25 | | 1.9 to 4.5 | 2.25 to 3.38 | | | 4.5 to 6.0 |
| (21) Zinc ion-maneb complex [Ref. I-Z-04-00.08] | 3.2 to 6.4 | 3.2 to 6.4 | | 3.2 to 6.4 | 3.2 to 6.4 | | 6.4 | 4.8 to 6.4 |
| (22) Zineb [Ref. I-Z-10-00.12] | | | | | 1.5 | | 1.0 to 1.5 | |

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*Cadmium resistant stains of this pathogen are common.

### C. Comparative effectiveness and impact

(1) Mercury compounds have a broad spectrum of turf pathogen control at high efficiency for low dosage rates. Substitute compounds are usually used in combination to achieve broad spectrum control at higher dosage rates, higher cost and more difficult application procedures.

(2) The impact of withdrawal of mercury for turf disease control will be very severe on some manufacturers, on golf greens management budgets and on turf quality.

## 9. Turf Weed Control (Crabgrass)

### A. Mercury compounds

Phenylmercuric acetate: [Ref. Reg. Nos. 702-14, 1001-14, 1001-24, 1439-173, etc.]

(a) 0.25 to 0.4 oz actual/1000 sq ft.

(b) 0.0003 oz actual plus 0.1391 oz dimethylamine salt of 2, 4-D and 0.005 oz isopropyl N-(3-chlorophenyl) carbamate/1000 sq ft.

(c) 0.009 oz actual plus 2.25 oz Thiram/1000 sq ft.

### B. Substitute compounds

(1) Octyl ammonium methanersenate plus dodecylammonium methanearsenate [Ref. Reg. No. 2853-6] 0.64 oz actual each of /1000 sq ft.

(2) Calcium methanearsenate [Ref. Reg. Nos. 264-147 and 2853-4] 0.83 oz actual/1000 sq ft.

(3) Disodium methanearsenate: [Ref. Reg. No. 572-199] 0.76 oz actual/1000 sq ft.

(4) Monosodium acid methanearsenate: [Ref. Reg. No. 728-79] 0.52 oz actual/1000 sq ft.

### C. Comparative Effectiveness and Impact

(1) Substitute materials are about equal to mercury for crabgrass control in post-emergence application and are safer from point of view of injury to desirable grasses.

(2) Other substitute materials are available for use before crabgrass emerges.

(3) Impact of withdrawal of mercury for this use will be minimal.

## 10. Turf Weed Control (moss)

### A. Mercury compounds

(1) Phenylmercuric acetate: [Ref. Reg. Nos. 538-5, 24, 36] 0.02 to 0.51 oz actual/1000 sq ft.

(2) Phenylmercuric triethanol ammonium lactate: [Ref. Reg. No. 802-233] 0.17 to 0.5 oz actual/1000 sq ft.

### B. Substitute compounds

(1) Ferrous ammonium sulfate: [Ref. Reg. No. 7923-3] 9.8 lb actual/100 sq ft.

(2) Ferrous sulfate: [Ref. Reg. No. 7404-3] 2.0 lb actual/1000 sq ft.

(3) Ferrous sulfate heptahydrate: [Ref. Reg. No. 5584-17] 1.5 lb actual/1000 sq ft.

### C. Comparative effectiveness and impact

(1) Substitute materials are equally effective for moss control but require much higher dosage.

(2) Impact of withdrawal of mercury for moss control will be minimal.

## VIII. Paper (mold resistant)

### 1. Mercury compounds

Phenylmercuric acetate: [Ref. I-P-08-00.10]

A. Beater application: 0.8 lb/ton of fiber, dry weight.

B. Coating application: 0.1 to 0.3 lb/side/ton or 150 to 225 ppm as a spray.

C. Calender application: 0.1 to 0.3 lb/side/ton or 0.5% solution.

### 2. Substitute compounds

A. Alkyl dimethyl benzyl ammonium chlorides and Bis (tributyltin) oxide: [Ref. I-A-08-15.02]

(1) 3750 ppm quaternary alone.

(2) 5000 ppm quaternary plus 250 ppm TBTO.

(3) 625 to 2500 ppm quaternary plus 125 to 500 ppm TBTO.

B. Captan:
0.15 to 0.90% by weight.

C. 4-Chloro-3, 5-Xylenol: [Ref. I-C-21-00.02] Use as required.

D. Copper 8-quinolinolate: [Ref. I-C-34-00.02] Use as required or 0.04% metallic copper equivalent in wax sizing.

E. Diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride: [Ref. I-D-13-00.01] Use 0.4% of a mixture of 40.9% quaternary plus 11.7% tributyltin salicylate based on dry weight of solids; or use 0.5 of above in the tub size.

F. N-Dodecylguanidine hydrochloride: [Ref. I-D-27-80.01] 0.4 to 0.8% on weight of paper.

G. Dodine: [Ref. I-D-28-00.04] 0.8% on weight of paper.

H. 2, 2'-Methylenebis-(3, 4, 6-trichlorophenol): [Ref. I-M-13-00.03] 0.02 to 0.25% on weight of paper.

I. Sodium dimethyldithiocarbamate: [Ref. I-S-09-00.05] 0.455 to 0.911% plus 0.04 to 0.08% sodium 2-mercaptobenzothiazole based on weight of sheet.

J. Sodium pentachlorophenate: [Ref. I-S-15-00.03] 0.1 to 0.5% based on weight of sheet.

K. Sodium o-phenylphenate: [Ref. I-S-16-00.09] 0.1 to 0.3% on weight of stock.

L. Thiram: [Ref. I-T-10-00.08] 0.3 to 1.2% plus 0.3 to 1.2% of zinc pentachlorophenate based on weight of finished paper.

M. 3, 4' 5-Tribromosalicylanilide: [Ref. I-T-11-00.01] 0.025 to 0.25% or 200 or more ppm based on weight of paper.

N. Ziram: [Ref. I-Z-11-00] 0.46 to 0.86% plus 0.02 to 0.037% zinc-2-mercaptobenzothiazole on weight of sheet.

### 3. Comparative effectiveness and impact

A. Mercury compounds are highly effective at low concentrations. Substitute materials require higher dosages.

B. Mercury compounds are colorless. Some substitute compounds impart undesirable colors, others do not.

C. Substitute compounds appear to be adequate.

D. Impact on industry will be very small, none on consumer.

## IX. Plastics

### 1. Plastics (unspecified)

#### A. Mercury compounds

(1) Phenylmercuric acetate: [Ref. I-P-08-00.01] Fungistatic surface treatment: 150 to 225 ppm spray.

(2) Phenylmercuric borate: [Ref. I-D-13-00.04] Fungistatic film: 50 ppm phenylmercuric borate plus 31.25 ppm diisobutylphenoxy - ethoxyethyl dimethyl benzyl ammonium chloride by weight of pellets before molding.

(3) Phenylmercuric propionate: [Ref. I-P-15-00.01] Fungistatic disposable bags for garbage and other wastes: 0.02% by weight.

B. **Substitute compounds**

(1) Alkyl dimethyl benzyl ammonium chloride: [Ref. I-A-08-15.02] Fungistatic surface treatment: 5000 ppm plus 250 ppm TBTO.

(2) Bis (tributyltin) sulfosalicylate: [Ref. I-B-12-00.01] 0.05% by weight or as required.

(3) 4-Chloro-3, 5-xylenol: [Ref. I-C-21-00.02] Use as required.

(4) 3,4', 5-Tribromosalicylanilide: [Ref. I-T-11-00.02]

(5) Tributyltin linoleate: [Ref. I-T-12-50.01] 0.43%, more or less as required, by weight of resin.

(6) Tributyltin monopropylene glycol maleate: [Ref. I-T-12-60.01]

(a) For floor tile use 0.8% by weight of plasticizer.

(b) For calendered film use 0.2 to 1.0% by weight of plasticizer.

C. **Comparative effectiveness and impact**

(1) Higher concentrations of substitute compounds at higher costs are needed to secure adequate protection in place of mercury.

(2) Relative spectrums of microorganism control not known.

(3) Impact on manufacturer and consumer not known but probably insignificant, since no replies were received to our December 3, 1970, Federal Register request for comments and views.

### 2. Plastics (polyethylene)

A. **Mercury compounds**

Phenylmercuric borate: [Ref. I-P-08-10.01] 50 ppm PMB plus 31.25 ppm diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride by weight of pellets before molding. Fungistat.

B. **Substitute compounds**

(1) Captan: [Ref. I-C-10-00.16] 0.44 to 1.74% by weight of stabilizer.

(2) Ziram: [Ref. I-Z-11-00.07] 0.225% plus 0.0195% of zinc 2-mercaptobenzothiazole by weight of resins.

C. **Comparative effectiveness and impact**

(1) Substitute compounds require dosage rates of 85 to 248 times that of mercury for effective fungal control.

(2) Relative spectrums of microorganism control are unknown.

(3) Impact on withdrawal of mercury for this use is unknown but assumed to be minimal.

### 3. Plastics (polystyrene)

A. **Mercury compounds**

Phenylmercuric borate: [Ref. I-P-08-10.01] 50 ppm PMB plus 31.25 ppm diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride by weight of pellets before molding. Fungistat.

B. **Substitute compounds**

Ziram: [Ref. I-Z-11-00.07] 0.255% plus 0.0195% of zinc 2-mercaptobenzothiazole by weight of resin.

C. **Comparative effectiveness and impact**

(1) Substitute compound requires dosage rate 85 times that of mercury for comparable effectiveness.

(2) Relative spectrums of microorganism control are unknown.

(3) Impact of withdrawl of mercury use is unknown but assumed to be minimal.

### 4. Polyvinyl Chloride Film (bacteriostatic at surface)

#### A. Mercury compounds

Phenylmercuric propionate (0.62%): [Ref. Reg. No. 7101-2] Product is disposable plastic bag impregnated with mercurial and bearing bacteriostatic (bacterial growth inhibiting) claim.

#### B. Substitute compounds

(1) Captan (N-trichloromethylthio-4-cyclohexene-1, 2-dicarboximide) (90%): [Ref. Reg. No. 1965-11] 0.2 to 0.5% product by weight of total formula.

(2) 4-chloro-3, 5-xylenol (100%): [Ref. Reg. No. 4026-4] Recommended for "plastics" but no dosages available.

(3) Tri-n-butyltin linoleate (75%): [Ref. Reg. No. 5204-15] 0.15 to 0.2% product by weight based on plastic mix weight.

(4) Diphenylstibine 2-ethylhexoate (10%): [Ref. Reg. No. 5204-42] 1.3 to 5% product based on weight of film.

(5) Tributyltin linoleate (98%): [Ref. Reg. No. 8314-4] 0.43% product by weight of plastic mix.

(6) 3, 4, 5-Tribromosalicylanilide (97%) and 3, 5 Dibromosalicylanilide (2%): [Ref. Reg. No. 6390-29] 2.0% product based on total weight of media.

#### C. Comparative effectiveness and impact

(1) Substitute compounds appear to be more than adequate.

(2) Impact on industry and consumer appears to be nil.

### 5. Vinyl (bacterial preservatives)

#### A. Mercury compounds

Phenylmercuric hydroxide (17%): [Ref. Reg. No. 6516-3] Vinyl (otherwise unidentified) coating for fabrics, ground together with chlorinated paraffin: 0.5 lb product/99.5 lb media.

#### B. Substitute compounds

(1) Diphenylstibine 2-ethylhexoate (10%): [Ref. Reg. No. 5204-42] Polyvinyl chloride: 1.3 to 5% product by weight.

(2) Captan (N-trichloromethylthio-4-cyclohexene-1, 2-dicarboximide) (90%): [Ref. Reg. No. 1965-11] Polyvinyl chloride: 0.2 to 0.5% product by weight.

(3) Bis (tri-n-butyltin) oxide (.075%) and alkyl (61%$C_{12}$, 23%$C_{14}$, 11%$C_{16}$, 5%$C_8$-$C_{18}$) dimethyl benzyl ammonium chlorides (1.5%): [Ref. Reg. No. 3090-137] 1 part product to 2 parts water, "spray surface uniformly."

#### C. Comparative effectiveness and impact

(1) Substitute compounds appear to be adequate.

(2) Impact on industry expected to be minimal. Cost to consumer expected to increase.

## X. Rubber

### 1. Fungistats

#### A. Mercury compounds

(1) Phenylmercuric acetate: [Ref. I-P-08-00.10] Fungistat: 125-225 ppm, spray surfaces.

(2) Phenylmercuric borate: [Ref. I-D-13-00.02 and I-P-08-10.01] Fungistat: 50 ppm plus 31.25 ppm. diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride, before molding.

#### B. Substitute compounds: [Ref. I-Z-08-15. .01]

(1) Alkyl dimethyl benzyl ammonium chloride and Bis (tributyltin) oxide: [Ref. I-

A-08-15.01] 5000 ppm quaternary and 250 ppm TBTO, spray surfaces.

(2) Bis (tributyltin) sulfosalicylate: [Ref. I-B-12-00.01] 0.5% by weight of rubber.

(3) 4-Chloro-3, 5-xylenol: [Ref. I-C-21-00.02] As required.

(4) Dehydroabietylamine pentachlorophenate: [Ref. I-D-02-00.01] 0.5 to 1.0% by weight.

(5) Salicylanilide: [Ref. I-S-01-00.01] 0.5% by weight.

(6) Ziram: [Ref. I-Z-11-00.07] 0.5% by weight of formulation containing 46% ziram plus 4% zinc-2-mercaptobenzothiazole.

### 2. Bacteriostats

#### A. Mercury compounds

Phenylmercuric hydroxide (17%): [Ref. Reg. No. 6516-3] Chlorinated rubber coatings for fabrics: 0.5 lb product/99.5 lb media.

#### B. Substitute compounds

(1) Ziram (Zinc dimethyldithiocarbamate) and Zinc 2-mercaptobenzothiazole (total Zn metallic 19.8%): [Ref. Reg. No. 1965-19] 0.2 to 1.5% product by weight of finished media.

(2) 1-(3-chloroallyl)-3, 5, 7-triaza-1-azoniaadamantane chloride (90%): [Ref. Reg. No. 464-327]0.5 to 0.15% product by weight.

(3) Sodium pentachlorophenate (90%): [Ref. Reg. No. 464-125] 0.3% product by weight.

(4) Sodium o-phenylphenol: [Ref. Reg. No. 464-78] 0.3% product by weight.

(5) Captan (N-trichloromethylthio-4-cyclohexene-1, 2-dicarboximide (90%): [Ref. Reg. No. 1965-11] 0.4% product by weight of latex.

(6) Dehydroabietylamine pentachlorophenate (45%): [Ref. Reg. No. 2829-55] 0.5 to 1% active ingredient based on weight of finished product.

(7) 4-chloro-3, 5-xylenol (100%): [Ref. Reg. No. 4026-4] Product recommended for neoprene and rubber preservation, no dosages stipulated.

#### C. Comparative effectiveness and impact

(1) Substitutes appear to be adequate.

(2) Impact on industry expected to be minimal.

(3) Cost to consumer expected to increase.

## XI. Sanitizers

### 1. Dust and cleaning cloth (bacteriostatic)

#### A. Mercury compounds

Phenylmercuric oleate (0.01%): [Ref. Reg. No. 8618-1] Product inpregnated into fabric using mineral oil.

#### B. Substitute compounds

(1) Dilauryl dimethyl ammonium bromide (0.25%): [Ref. Reg. No. 303-56] 1 fluid ounce/6 inches mop or cloth.

(2) n-Alkyl (50%$C_{12}$, 30%$C_{14}$, 17%$C_{16}$, 3%$C_{18}$) dimethyl ethylbenzyl ammonium chloride, and n-alkyl (60%$C_{14}$, 30%$C_{16}$, 5%$C_{12}$, 5%$C_{18}$) dimethylbenzyl ammonium chlorides. (0.2% total): [Ref. Reg. No. 1270-92] 1 fluid ounce/6 inches of mop or cloth.

(3) Lauryl pyridinium salt of 5-chloro-2-mercaptobenzothiazole: [Ref. Reg. No. 1750-42] Spray on cloth undiluted.

(4) Dialkyl (1%$C_6$, 8%$C_8$, 7%$C_{10}$ 48%$C_{12}$, 17%$C_{14}$, 9%$C_{16}$, 10%$C_{18}$) dimethyl ammonium chloride: [Ref. Reg. No. 1878-9] Mix 1 1/2 gal product with 55 gal mineral oil and add 2.5 to 3 gal/100 lb dry weight cloth.

(5) 2, 2'-methylenebis (3, 4, 6-trichlorophenol) (0.5%): [Ref. Reg. No. 2915-29] 6 to 16 ounces per mop depending on size.

(6) o-benzyl-p-chlorophenol (1.0%): [Ref. Reg. No. 4878-17] Used undiluted as a dip.

(7) 4-and 6-chloro-2-phenylphenol (1.0%): [Ref. Reg. No. 6831-5] 25 fluid ounces/100 lb dry cloth.

### C. Comparative effectiveness and impact

(1) Substitute compounds are adequate.

(2) Impact on industry and consumer expected to be negligible.

## 2. Floor Covering Finishes (bacteriostatic)

### A. Mercury compounds

Phenyl mercuric acetate (0.025%): [Ref. Reg. No. 52-145] Used undiluted for institutional floor care.

### B. Substitute compounds

(1) 2, 2' methylenebis (3, 4, 6-trichlorophenol): [Ref. Reg. No. 824-1] 1% to 4% product by weight of media.

(2) Alkyl (derived from fatty acids of coconut oil) amine hydrochlorides: [Ref. Reg. No. 4313-37] 0.063% product by weight of media.

(3) Sodium pentachlorophenate (79%): [Ref. Reg. No. 464-299] 0.025 to 0.15% product by weight of formulation.

(4) 1-(3-chloroallyl)-3, 5, 7-triaza-1-azoniaadamantane chloride (90%): [Ref. Reg. No. 464-327] 0.025% product by weight of formulation.

(5) 4-chloro-3, 5, -xylenol (100%): [Ref. Reg. No. 4026-4] Dosage not stated.

### C. Comparative effectiveness and impact

(1) Substitute compounds are adequate.

(2) Impact on industry and consumer expected to be negligible.

## 3. Floor Wax (bacteriostatic)

### A. Mercury compounds

Phenyl mercuric acetate: [Ref. Reg. No. 52-145] Applied to floor undiluted.

### B. Substitute compounds

(1) 2-Bromo-2-nitropropane-1, 3-diol: [Ref. Reg. No. 1839-60] .05 to 0.1% product by weight of formula.

(2) Dialkyl (1%$C_6$, 8%$C_8$, 7%$C_{10}$, 48%$C_{12}$, 17%$C_{14}$, 9%$C_{16}$, 10%$C_{18}$) dimethyl ammonium chloride: [Ref. Reg. No. 1839-8] 1.5 to 2% product by weight of formula.

(3) 1-(3-chloroallyl)-3, 5, 7-triaza-1-azoniaadamantane chloride: [Ref. Reg. No. 464-327] 0.025% product by weight of formula.

(4) 4-chloro-3, 5-xylenol: [Ref. Reg. No. 4026-4] Dosage not specified.

(5) 2, 2' - methylenebis (3, 4, 6-trichlorophenol): [Ref. Reg. No. 824-1] 1 to 4% product by weight of formulation.

(6) 2, 2'-methylenebis (4-chlorophenol): [Ref. Reg. No. 824-6] 1 to 7% product by weight of formulation.

### C. Comparative effectiveness and impact

(1) Substitute compounds are adequate.

(2) Impact on industry and consumer expected to be nil.

# XII. Seed Treatments - Field Crops

**A. Mercury compounds:**

Phenylmercuric acetate-see tables 1 through 7, attached.

**B. Substitute compounds:**

see tables 1 through 7, attached

### XII. Seed Treatments

#### 1. Barley

| | Phenylmercuric acetate | Captan | Maneb | Paraformaldehyde | Thiram | Vitavax (carboxin)[1] | Zinc ion-maneb complex | Zineb[2] | | Formaldehyde |
|---|---|---|---|---|---|---|---|---|---|---|
| | ounces actual per bushel | | | | | | | | | p.p.m. |
| Black loose smut, covered smut | 0.019 to 0.038 | | 0.75–2.10 | 0.18 | 2.04 | 1.5 | 1.6 | | | 1200 to 1600 |
| Damping-off, seed decay, seedling blights | 0.019 to 0.038 | 1.2–1.9 | 0.75–2.10 | | 2.04 | | 1.6 | 0.42–0.5 | | |
| Stripe | 0.019 to 0.038 | | | | | | | | | |

### XII. Seed Treatments

#### 2. Cotton

| | Phenylmercuric acetate | Busan 72[1] | Captan | Chloranil[2] | Chloroneb | Dexon[3] | Maneb | Monosodium salt of hexachlorophene | PCNB | Terrazole (R)[4] | Thiram | Zineb[5] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ounces actual per 100 pounds | | | | | | | | | | | |
| Sore shin | 0.075 to 0.338 | 3.0–3.5 | | | 6.5 | | | | 4.0 to 6.0 | 1.0 to 2.5 | | |
| Surface seed-borne anthracnose | 0.075 to 0.338 | | | | | 1.4–2.1 | | | | | | |
| Damping-off, Seed rot and decay, seedling blights | 0.075 to 0.338 | 3.0–3.5 | 2.7–4.0 | 2.9–5.7 | 6.5 | 1.4–2.1 | 9.6 | 0.9 to 1.3 | 4.0 to 6.0 | 1.0 to 2.5 | 1.89 to 3.00 | 0.84 to 2.94 |

[1] 2-(Thiocyanomethylthio) benzothiazole

[2] Used as a supplement to suitable standard seed treatments.

[3] p-(Dimethylamino) benzenediazo sodium sulfonate.

[4] 5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole. with PCNB.

[5] Used in combination with Captan.

## XII. Seed Treatments

### 3. Flax

| | Phenylmercuric acetate | Captan | Chloranil[1] | Maneb | Thiram | Zinc ion-maneb complex | Zineb[2] |
|---|---|---|---|---|---|---|---|
| | ounces actual per bushel | | | | | | |
| Damping-off,<br>Root Rots,<br>Seed decay | 0.057<br>to<br>0.114 | 1.02<br>to<br>1.46 | 2.05<br>to<br>2.21 | 0.75<br>to<br>3.20 | 1.45 | 2.4<br>to<br>3.2 | 0.95<br>to<br>1.26 |

[1] Used only as supplemental treatment to suitable standard seed protectants.
[2] Used only in combination with Captan.

## XII. Seed Treatments

### 4. Oats

| | Phenylmercuric acetate | Captan | Chloranil[1] | Maneb | Paraformaldehyde | Zineb[2] | Formaldehyde |
|---|---|---|---|---|---|---|---|
| | ounces actual per bushel | | | | | | |
| Leaf stri | 0.019<br>to<br>0.038 | | | | | | |
| Seed decay<br>Seedling blights | | 0.48<br>to<br>0.90 | 1.92 | 0.75<br>to<br>2.10 | | | |
| Covered smut,<br>Loose smut | | | | 0.75<br>to<br>2.10 | 0.18 | 0.47<br>to<br>0.53 | 1200<br>to<br>1600 |

[1] Used as supplemental treatment to suitable standard treatments.
[2] In combination with Captan.

## XII. Seed Treatments

### 5. Rice

| | Phenylmercuric acetate | Captan | Chloranil[1] | Copper-zinc-chromate complex | Dichlone | Thiram | Zinc ion-maneb complex |
|---|---|---|---|---|---|---|---|
| | ounces actual per 100 pounds | | | | | | |
| Damping-off,<br>Seed rots | 0.042<br>to<br>0.084 | 1.7-3.75 | 1.9-2.4 | 7.2 | 1.0 | 1.55-3.3 | 1.6-3.2 |

[1] Used only as a supplemental treatment to suitable standard seed protectants.

## XII. Seed Treatments

### 6. Sorghum

| | Phenylmercuric acetate | Captan | Chloronil[1] | Dexon[2] | Dichlone | Difolatan (captafol) | Hexachlorobenzene | PCNB | SDDC + SMBT[3] | Terrazole(R)[4] | Thiram | Zineb | Copper carbonate | Formaldehyde |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ounces actual per 100 pounds | | | | | | | | | | | | oz. Cu/100$^{-16}$ | |
| Covered kernel smut, Loose smut | 0.019 to 0.038 | 1.9-3.0 | | 0.7-1.4 | | | 0.57-1.34 | 2.4[1] | 2.57 | | 1.34-1.79 | | 1.07-1.43 | 1200 to 1600 |
| Damping-off, Seed decay | 0.019 to 0.038 | 1.9-3.0 | 1.9-2.9 | 0.7-1.4 | 1.0 | 1.8-2.3 | 0.57-1.34 | 0.5[2] | | 0.125 | 1.34-1.79 | 1.32-1.41 | | |

[1] In combination with Dexon.
[2] In combination with Terrazole.
[3] Used only as a supplement to suitable standard seed treatments.
[4] p-(Dimethylamino) benzenediazo sodium sulfonate.
[5] 27.6% Sodium dimethyl dithiocarbamate + 2.4% Sodium 2-mercaptobenzothiazole.
[6] In combination with PCNB.
[7] In combination with Captan.

## XII. Seed Treatments

### 7. Wheat

| | Phenylmercuric acetate | Captan | Hexachloro-benzene | Maneb | PCNB | SDDC + SMBT[1] | Terrazole[2] | Thiram | Vitavax[3] | Zinc ion-maneb complex | Zineb[4] | Copper carbonate | Copper sulfate Basic | Formaldehyde |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ounces actual per bushel | | | | | | | | | | | oz. copper/bushel | | p.p.m. |
| Dwarf bunt, Bunt (stinking smut) Flag smut, covered smut | 0.019 to 0.038 | 0.66 to 1.20 | 0.20 to 0.53 | 0.75 to 2.10 | 0.50 to 0.75 | 1.44 | 0.125 | 1.0 | 1.8 | 1.6 | 0.47 to 0.52 | 0.4-0.8 | 1.0-2.0 | 1200 to 1600 |
| Kernel smudge | 0.019 to 0.038 | | | | | | | | | | | | | |
| Seed decay, Seedling blights | 0.019 to 0.038 | 0.66 to 1.20 | | 0.75 to 2.10 | 0.50 to 0.75 | | 0.125 | 1.0 | | 1.6 | 0.47 to 0.52 | | | |

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[1] 27.6% Sodium dimethyl dithiocarbamate + 2.4% Sodium 2-mercaptobenzothiazole.

[2] In combination with PCNB.

[3] Limited to foundation and registered seed.

[4] In combination with Captan.

C. **Comparative effectiveness and impact;**

(1) Mercury as PMA is the only available control for stripe (*Helminthosporium*) of barley.

(2) Mercury compounds are broad spectrum fungistats for a wide range of pathogens on field crop seeds. They control several diseases for which label claims have never been noted, such as certain bacterial pathogens on cotton seed and fusarium scab of cereals.

(3) Mercury as PMA is effective at 0.1 to 0.01 of the concentration of substitute materials.

(4) The impact on withdrawal of these uses for PMA would be severe and result in greatly increased costs to the commercial seed treater, the farmer and consumer of crops grown from the treated seed.

D. An estimation of the potential use of PMA for the preceeding seven field crops is given in table 8.

**Table 8. Estimated Potential Use of Phenylmercuric Acetate Field Crop Seed Treatments – Based On 1969 Seed Requirements**

| Crop Seed | Seed Used – 1969 | PMA | Hg |
|---|---|---|---|
| | X 1,000 | lb. act. X 1,000 | lb. X 1,000 |
| Barley | 16,000 bu. | 2.46 | 1.47 |
| Cotton | | | |
| acid delinted | 95, 184 lb. | 671.05 | 399.74 |
| reginned | 179,897 lb. | 1,902.42 | 1,133.27 |
| fuzzy | 11,422 lb. | 181.18 | 107.93 |
| Flax | 72 bu. | 0.64 | 0.38 |
| Oats | 59,563 bu. | 106.10 | 63.20 |
| Rice | 2,119 bu. | 0.08 | 0.05 |
| Sorghum | 129,041 lb. | 4.10 | 2.45 |
| Wheat | 1,552 bu. | 3.40 | 2.03 |
| Totals | | 2,871.43 | 1,710.52* |

*Note that the Pesticide Review – 1970 shows that only 204,364 pounds of mercury was used in 1969 for all agricultural purposes. Assuming that all of the 204,364 pounds was used for treating seed, only about 8 percent of the seed was treated with mercury.

## XII. Seed Treatments

### 8. Flower Seeds

A. Mercury compounds:

[Ref. I-N-06-00.02]

Hydroxymercurichlorophenol Ornamental Seed and Bulb Treatments

| Name of Seed | Treatment | | Name of Seed | Treatment | |
|---|---|---|---|---|---|
| | Avdp. oz. 28.6% per 15 pounds seed | Soak time in normal solution | | Avdp. oz. 28.6% per 15 pounds seed | Soak time in normal solution |
| Acroclinium | 1 oz. | ---- | Aquilegia | ½ oz. | 60 min. |
| Ageratum | 1 oz. | 60 min. | Arabis alpina | 1 oz. | 60 min. |
| Agrosteman | 1 oz. | 60.min. | Arctotis | 1 oz. | 90 min. |
| Amaranthus | ½ oz. | 30 min. | Aster | 1 oz. | 60 min. |
| Antirrhinum (snapdragon) | ½ oz. | 60 min. | Balsam | ½ oz. | 30 min. |
| | | | Browallia | 1 oz. | 30 min. |

| Name of Seed | Treatment |  |
|---|---|---|
|  | Avdp. oz. 28.6% per 15 pounds seed | Soak time in normal solution |
| Calendula | 1 oz. | 60 min. |
| Calla Lily | --- | 60 min. |
| Campanula | 1 oz. | 30 min. |
| Carnary Bird Flower | 1 oz. | 60 min. |
| Canterbury | --- | 15 min. |
| Cardiospermum | ½ oz. | 60 min. |
| Carnation | 1 oz. | 30 min. |
| Celosia plumosa | 1 oz. | 30 min. |
| Centaurea | 1 oz. | 30 min. |
| Chrysanthemum | 1 oz. | 30 min. |
| Clarkia | ½ oz. | 60 min. |
| Clematis | 1 oz. | 60 min. |
| Convolvulus | 1 oz. | 60 min. |
| Coreopsis | 1 oz. | 30 min. |
| Cosmos | ½ oz. | ---- |
| Crimson Flax | 1 oz. | ---- |
| Crocus | --- | 2 hrs. |
| Daffodil (bulb) | --- | 2 hrs. |
| Dahlia (Tuber) | --- | 30 min. |
| Dahlia (Seed) | ½ oz. | ---- |
| Delphinium | 1 oz. | 30 min. |
| Digitalis | 1 oz. | 30 min. |
| Dimorphoteca | ½ oz. | ---- |
| Eschscholtzia | 1 oz. | 90 min. |
| Four O'Clock | 1 oz. | 60 min. |
| Freesia (Corms) | --- | 60 min. |
| Gaillardia | 1 oz. | 15 min. |
| Geum | 1 oz. | ---- |
| Gladiolus (Corms) | --- | 7 hrs.[2] |
| Globeamaranth | --- | 30 min. |
| Godetia | 1 oz. | 60 min. |
| Gypsophila | 1 oz. | 60 min. |
| Helianthus | 1 oz. | 30 min. |
| Helichrysum | 1 oz. | 30 min. |
| Heliotrope | 1 oz. | 60 min. |
| Hibiscus | 1 oz. | 90 min. |
| Hollyhock | 1 oz. | 30 min. |
| Humulus | 1 oz. | 60 min. |
| Hyacinth (bulb) | --- | 2 hrs. |
| Ipomeoa | 1 oz. | 60 min. |
| Jonquil (bulb) | --- | 2 hrs. |
| Kochia | ½ oz. | 30 min. |
| Kudzu Vine | 1 oz. | 60 min. |
| Larkspur | 1 oz. | 60 min. |
| Lavatera | 1 oz. | 60 min. |
| Lupinus | ½ oz. | 60 min. |
| Marigold | ½ oz. | 60 min. |
| Mignonette | ½ oz. | 60 min. |
| Myosotis | ½ oz. | 60 min. |
| Narcissus (bulb) | --- | 2 hrs.[3] |
| Nasturtium | 1 oz. | 30 min. |
| Pansy | 1 oz. | 30 min. |
| Peony (Roots) | --- | 30 min.[1] |
| Petunia | ½ oz. | 30 min. |
| Phlox | 1 oz. | 30 min. |
| Poppy | ½ oz. | 30 min. |
| Portulaca | ½ oz. | 30 min. |
| Pyrethrum | ½ oz. | 30 min. |
| Salpiglossis | 1 oz. | 60 min. |
| Salvia | ½ oz. | 30 min. |
| Scabiosa | 1 oz. | 60 min. |
| Stevia | 1 oz. | 60 min. |
| Stock | ½ oz. | 30 min. |
| Sweet Alyssum | ½ oz. | 60 min. |
| Sweet Pea | 1 oz. | 30 min. |
| Sweet William | 1 oz. | 30 min. |
| Tuberose (bulb) | --- | 30 min. |
| Tulip (bulb) | --- | 2 hrs. |
| Valerian | 1 oz. | 30 min. |
| Verbena | 1 oz. | 30 min. |
| Violet | 1 oz. | 30 min. |
| Wallflower | 1 oz. | 30 min. |
| Zinnia | 1 oz. | 60 min. |

[1] Preplanting treatment only.
[2] Use extra strength solution.
[3] Use double strength solution.

### B. Substitute compounds:

Thiram: [Ref. I-T-10-00.08] dust thoroughly with 4 to 12% dusts

### C. Comparative effectiveness and impact:

(1) Mercury compounds are more effective than the available substitute com-

pounds for controlling most seed-borne pathogens and some soil-borne organisms.

(2) The impact of withdrawal of mercury for these uses will be minimal.

(3) Note: The manufacturer has already ceased production of this chemical. Registrations are now continued in effect only to cover merchandise in channels of trade.

## PESTICIDE USES OF MERCURY

### XIII. Surfaces (fungistats)
### (see also XI. Sanitizers)

1. Fungistats on Commercial, Institutional and Household Surfaces e.g. [cabinets, floors, walls, ceilings, garbage cans, lockers, masonry, tile, refrigerator and other hard surfaces; blankets, canvas goods, carpeting, clothing, cubicle curtains, hampers, laundry bags, leather goods, linens, mattresses, uniforms, upholstery and similar porous surfaces.]

A. **Mercury compounds**

20 ppm of Sodium ethylmercurithiosalicylate plus 4860 ppm alkyl dimethyl benzyl ammonium chloride, 360 ppm tributyltin benzoate, 240 ppm tributyltin isopropyl succinate, 120 ppm tributyltin linoleate and 250 ppm isopropyl alcohol, applied as a low-pressure bomb spray. [Ref. I-A-08-25.04]

B. **Substitute compounds**

(1) Alkyl dimethyl benzyl ammonium chlorides: [Ref. I-A-08-00.01, I-A-08-15.01, I-A-08-20.01, I-A-08-25.04, I-A-08-35.01, I-A-08-45.04, I-A-08-50.01] 200 to 30,000 ppm alone or in combination with a large number of other active ingredients as low pressure bomb sprays or by mopping, wiping or washing.

(2) Alkyl dimethyl benzyl ammonium saccharinate: [Ref. I-A-11-00.01]

(a) 400 ppm plus 100 ppm sodium o-phenylphenate by mop or spray.

(b) 10,000 ppm plus 2500 ppm sodium o-phenylphenate and 237,000 ppm isopropanol by low pressure bomb.

(3) Aklyl dimethyl 3, 4-dichlorobenzyl ammonium chloride: [Ref. I-A-14-20.01] 700 ppm plus 138 ppm tributyltin benzoate and isopropanol by mop, sponge, brush or spray.

(4) Alkyl dimethyl ethylbenzyl ammonium cyclohexyl sulfamate: [Ref. I-A-17-00.01] 3,000 to 3,200 ppm plus 645, 000 to 675,500 ppm ethyl alcohol and 50,000 ppm propylene glycol by low-pressure bomb spray.

(5) Ammonium hydroxide-$C_8$ Fatty acid-Silver Complex: [Ref. I-A-32-00.01] 860 ppm metallic silver equivalent as a low-pressure bomb spray.

(6) Bis (tributyltin) oxide: [Ref. I-B-09-00.01] 420 ppm in low-pressure bomb spray.

(7) Calcium hypochlorite: [Ref. I-C-07-00.01] 7300 ppm by brush or sponge. Note: Not a substitute for residual properties of mercury compounds.

(8) Captan: [Ref. I-C-10-00.15] 375 ppm plus 240,600 ppm isopropanol as low pressure bomb spray.

(9) Chlorine dioxide: [Ref. I-C-13-60.01] 1000 ppm plus 292,000 ppm ethanol and 3000 ppm sodium carbonate as low pressure bomb spray. Note: Not a substitute for residual properties of mercury compounds.

(10) 4-Chloro-3, 5-xylenol: [Ref. I-C-21-00.01] 3300 ppm as a spray.

(11) Diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride: [Ref. I-D-13-00.01] 700 to 2000 ppm plus isopropyl alcohol or other agents.

(12) 80 percent methyldodecylbenzyl trimethyl ammonium chloride plus 20% **methyldodecylxylene bis (trimethyl ammonium chloride): [Ref. I-M-09-00.02]**

(a) 2000 to 5000 combined quaternaries plus 600,000 ppm ethanol as low pressure bomb spray, or

(b) 2500 to 5000 ppm combined quaternaries plus 750 to 2000 ppm brominated salicylanilides and 630,000 ppm ethanol or isopropanol as low-pressure bomb spray.

(13) 2, 2'-methylenebis-(3, 4, 5-trichlorophenol): [Ref. I-M-13-00.03] 200 ppm plus 400 ppm 2, 2' methylenebis (4-chlorophenol) as low pressure bomb spray.

(14) o-Phenylphenol:[Ref. I-P-19-00.03] 1000 to 2000 ppm plus various amounts of other fungistats, mostly as low-pressure bomb sprays.

(15) Sodium dimethyldithiocarbamate

(a) plus sodium 2-mercaptobenzothiazole [Ref. I-S-09-00.06]

(b) 1400 to 5800 ppm

(c) plus 120 to 500 ppm

(d) as wash, mop, sponge or spray.

(16) Sodium o-phenylphenate: [Ref. I-S-16-00.08] 1500 ppm plus 930 ppm methyl salicylate and 9300 ppm isopropanol as a spray.

(17) Zineb: [Ref. I-Z-10-00.15] 10,000 ppm as low-pressure bomb spray.

### C. Comparative effectiveness and impact

(1) Substitutes are available which are as effective as mercury compounds for fungistasis on surfaces.

(2) Impact of withdrawal of these uses will be slight to the consumer but may be more severe on the manufacturer.

## XIV. Tanneries (bacteriostats and fungistats)

### A. Mercury compounds

**Phenylmercuric acetate**

For hides and skins (in cellars of meat packing plants and tanneries): [Ref. I-P-08-00.09] 305 ppm solution of a combination of PMA, sodium pentachlorophenate and sodium trichlorophenate. For processing: [Ref. I-P-08-00.10 and I-P-08-00.11] soaking - 0.05 to 0.10 lb PMA (I) plus 0.25 to 0.50 lb potassium trichlorophenate (II)/1000 lb. Add to soak water. pickling - 0.03 lb (I) plus 0.15 to 0.25 lb II/1000 lb wet stock. Add to pickling solution.

Chrome tanning: 0.03 to 0.06 lb (I) plus 0.15 to 0.30 lb (II)/1000 lb wet stock. Add to chrome liquor.

Vegetable tanning: 0.03 to 0.06 lb (I) plus 0.15 to 0.30 lb (II)/1000 lb of tanned stock. Add to wash water or to final bleaching liquor.

Samming: Treat sawdust with 0.05 lb (I) plus 0.25 lb (II)/50 gal of water [120 ppm (I) plus 600 ppm (II)].

Fatliquoring: 500 to 1500 ppm (I) plus 2500 to 7500 ppm (II) on weight of fatliquor.

### B. Substitute compounds

(1) Pentachlorophenol: [Ref. I-P-05-00.03] 0.1 to 3.5% in processing solution or dressing formulations.

(2) 22.5% of potassium pentachlorophenate plus 22.5% of potassium 4 (or 6)-chloro-2-phenylphenate: [Ref. I-P-25-00.01]

Pickling: 0.1% by weight of stock. Chrome tanning: 0.1% by weight of stock. Vegetable tanning: 0.3% by weight of stock. Brusting, pearling or staining: 0.1% solution. Dying and fatliquoring: 0.1 to 0.2% solution.

(3) Sodium o-phenylphenate: [Ref. I-S-16-00.09] 0.1 to 3.5% by weight of processing solutions.

(4) 17.5% of sodium tetrachlorophenate plus 7.7% of sodium o-phenylphenate: [Ref. I-S-21-00.01]

Soaking: 1 to 2 lb/100 gal.

Pickling: 3 to 5 lb/1000 lb stock. Chrome and vegetable tanning: 3 to 5 lb/1000 lb stock.

(5) Tetrahydro-3, 5-dimethyl-2H, 1, 3, 5-thiadiazine-2-thione: [Ref. I-T-07-00.03]

Soaking: 2 to 4 oz/100 gal.

Padding, tanning, fatliquoring and coloring: 0.5 to 1.5 oz/100 gal.

Final rinse (leather to be used in clothing): 1.0 oz/100 gal.

(6) Tributyltin salicylate plus 40.9% Diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride and 6.5% isoprophanol: [Ref. I-D-13-00.03] Fatliquor and long bath: 0.5% of formulation by weight of leather.

### C. **Comparative effectiveness and impact**

(1) Substitute chemical products are more expensive than the mercury materials.

(2) We are not familiar with the various problems of color, hand and other quality factors which may influence the usability of substitute materials.

(3) Based on the fact that the industry failed to respond to the Federal Register request for views and comments, we believe that the impact of withdrawal of mercury registrations will have little impact on the tanning industry.

## XV. Wood

1. Logs, lumber (sap stain and mold during seasoning, storage and shipment):

### A. **Mercury compounds**

(1) Ethylmercury phosphate: [Ref. I-E-07-00.01] 150 to 300 ppm solution, or 72 to 1200 ppm plus sodium pentachlorophenate, or 225 to 450 ppm for heavy timbers.

(2) Phenylmercuric acetate: [Ref. I-P-08-00.08] 2 pints of 5% PMA plus 25% sodium trichlorophenate/75 gal (approximately 1600 ppm PMA).

(3) Phenylmercuric hydroxide: [Ref. I-P-09-50.01] 1 to 2 gal of 0.2% PMH plus 14.54% sodium pentachlorophenate and 3.16% sodium metaborate/40 to 50 gal.

(4) Phenylmercuric lactate: [Ref. I-P-10-00.01; I-S-15-00.02; I-S-21-00.01] Use 1 to 2 gal of 0.4% PML plus 1.0% sodium octaborate and 22.82% technical sodium pentachlorophenate/100 gal, 1 to 2 gal 0.4% PML plus 13.3% sodium metaborate and 22.82% technical sodium pentachlorophenate/100 gal, or 2 to 3 gal of 3.19% PML plus 49.23% sodium trichlorphenate/100 gal for western species including Douglas Fir, Hemlock and pine.

### B. **Substitute compounds**

(1) 2.0% Bis (tributyltin) oxide plus 4.5% 1-(Alkyl amino)-1, 3-amino propane monoacetate, 21.0% sodium tetrachlorophenate and 5.7% sodium salts of other chlorphenols: [Ref. I-A-07-00.01] 0.5 to 0.75% solution

(2) 2.5% o-Phenylphenol plus 2.5% pentachlorophenol: [Ref. I-P-19-00.02] dip in above formulation

(3) 14.4% Potassium pentachlorophenate plus 1.5% alkyl amino-3-aminopropane, 8.3% potassium trichlorophenate and 1.7% of other potassiums salts of chlorophenols: [Ref. I-P-25-00.02] Use 0.5 to 0.75% of above formulation in water. Dip or spray.

(4) 13 to 65% Sodium borate plus 27.7 to 36.0% sodium pentachlorophenate and 4.0 to 12.3% sodium carbonate: [Ref. I-S-04-00.01] 10 o 20 lb formulation/100 gal.

(5) Sodium pentachlorophenate: [Ref. I-S-15-00.02] 3 to 12 lb/100 gal.

(6) Sodium tetrachlorophenate: [Ref. I-S-21-00.01] 4.8 lb/100 gal.

### C. **Comparative effectiveness and impact**

(1) Mercury compounds are the most effective, require much smaller dosage rates and control more fungus species than the substitute materials. The mercury compounds are also much less expensive.

(2) The impact of withdrawal of mercury for this use will be great on the manufacturers of such formulations and will be very

great on the consuming lumber industry where federal specifications now require such treatment or where it is required by foreign purchasers of lumber.

### 2. Fence posts (rot and decay application)

#### A. Mercury compounds

(1) Mercuric chloride: [Ref. I-M-04-00.01] 1 tbs of 33.2% mercuric chloride plus 33.2% arsenious oxide/0.75 inch x 2.0 hole bored 6 inches above ground line, in green posts. Posts over 4 inches in diameter require 2 to 3 holes. Plug holes after filling. No access to livestock.

(2) Phenylmercuric oleate: [Ref. I-P-14-00.01] 1.0 to 1.25% solutions - soak

#### B. Substitute compounds

(1) Anthracene oil: [Ref. I-A-35-00.01] soak

(2) Coal for neutral oils: [Ref. I-C-22-00.01] soak.

(3) Copper naphthenate: [Ref. I-C-30-00.01] soak.

(4) Copper sulfate plus sodium fluoride or sodium chromate: [Ref. I-C-38-00.01] soak.

(5) Creosote (coal tar): [Ref. I-C-41-00.01] soak.

(6) Creosote (wood): [Ref. I-C-42-00.01] soak.

(7) Pentachlorophenol: [Ref. I-P-05-00.01] 5% solution, soak.

(8) 5.09% sodium dichromate plus 5.36% copper sulfate and 0.2% chromic acid solution: [Ref. I-S-07-50.01] soak.

(9) Tetrachlorophenol: [Ref. I-T-06-00.01] 5% solution, soak.

(10) Zinc naphthenate: [Ref. I-Z-05-00.01] 20% solution, soak.

#### C. Comparative effectiveness and impact

(1) Substitute compounds are at least as effective as mercury compounds for the control of rot and decay of fence posts.

(2) Substitute compounds frequently provide objectionable coloration to treated wood, mercury does not.

(3) Substitute compounds frequently impair the paintability of treated wood, mercury does not.

(4) Impact of withdrawal of mercury for treating fence posts will be negligible.

### 3. Lumber and timbers (rot and decay - consumer application)

#### A. Mercury compounds

(1) Phenylmercuric oleate: [Ref. I-P-14-00.01] 1.0 to 1.25% solution by brush, spray or dip.

(2) 0.6% Phenylmercuric oleate plus 7.125% technical pentachlorophenol: [Ref. I-P-14-00.01] brush, spray or dip.

#### B. Substitute compounds

See 2. B above. Apply by dip, spray or soak.

C. See 2. C above.

#### D. Addendum

##### (1) Mercury compounds

0.28% Phenylmercuric oleate plus 0.28% TBTO and 12.5% zinc naphthenate - household use by brush spray or dip. [Ref. Reg. No. 390-3]

## XVI. Dental and Surgical Instruments (disinfection)

### 1. Mercury compounds

A. Phenylmercuric borate (0.1%): [Ref. Reg. No. 1293-1] Instrument disinfectant used undiluted.

B. 3-(Hydroxymercuri)-4-nitro-o-cresol (0.48%): [Ref. Reg. No. 275-3] Disinfectant, used undiluted.

2. **Substitute compounds**

A. n-Alkyl ($60\%C_{14}$, $30\%C_{16}$, $5\%C_{12}$, $5\%C_{18}$) dimethylbenzym ammonium chloride (total 10%): [Ref. Reg. No. 859-7] Use-dilution: 1 fluid oz/2 gal water.

B. Potassium o-phenylphenate, and potassium o-benzyl-p-chlorophenate (and solubilizing and sequestering agents) (total 19.2%): [Ref. Reg. No. 1750-32] Use-dilution: 1-100.

C. Tetradecyl dimethyl benzyl ammonium chloride (1.25%), dodecyl dimethylbenzyl ammonium chloride (0.25%), and isopropyl alcohol (17.5%): [Ref. Reg. No. 3625-1] Use-dilution: 4 fluid oz product/gal water.

D. Isopropanol, and n-alkyl ($50\%C_{14}$, $40\%C_{12}$, $10\%C_{16}$) dimethylbenzyl ammonium chloride (total 29% actives): [Ref. Reg. No. 4330-1] Use-dilution: 1-32

E. Cresol, benzaldehyde, safrole, and formaldehyde (total 30% actives): [Ref. Reg. No. 5493-2] Use-dilution: 1-32.

F. Cresols, formaldehyde, phenylethyl, alcohol, and benzyl alcohol (total 95%): [Ref. Reg. No. 5493-4] Use-dilution: 2 fluid oz/gal of water.

G. Diisobutylcresoxyethoxyethyl-dimethylbenzyl ammonium chloride and o-phenylphenol ethoxynonyl-phenol complex (1.1%), and methyl-p-hydroxybenzoate (0.3%): [Ref. Reg. No. 7150-4] Use-dilution: 1 part product to 3 parts water.

3. **Comparative effectiveness and impact**

A. Substitute compounds are better disinfectants than mercury compounds.

B. No impact on industry or the consumer expected.

## XVII. Miscellaneous

1. **Broomcorn**

A. **Mercury compounds**

Phenylmercuric acetate: [Ref. I-P-08-00.09] 200 ppm in dye bath by weight of solution.

B. **Substitute compounds**

None.

C. **Impact**

(1) Broomcorn brooms and brushes must have a bright color and clean appearance to be saleable. A fungistatic agent with residual qualities is necessary in broom manufacture.

(2) Although no substitutes for mercury are registered for this use, it would appear that a suitable replacement compound could be found with little effort. Therefore, the impact of withdrawal of mercury for this use should be slight to moderate on the manufacturer and consumer.

2. **Cellulose sponges**

A. **Mercury compounds**

Phenylmercuric acetate: [Ref. I-P-08-00.09] 750 ppm solution.

B. **Substitute compounds**

None.

C. **Impact**

Unknown. Substitute compounds should not be difficult to find once the consumers are aware of the withdrawal of mercury for this use.

3. **Seam and bedding compounds (boat construction)**

A. **Mercury compounds**

Phenylmercuric oleate: [Ref. I-P-14-00.01] 400 ppm PMO plus 1425 ppm. Pentachlorophenol by volume of compound.

### B. Substitute compounds

None.

### C. Impact

Unknown. Mercury is thought to be of doubtful necessity or value in this use. Substitute materials should not be difficult to find.

## 4. Milk sample preservation (for dairy herd improvement)

### A. Mercury compounds

Mercuric chloride (32.2%): [Ref. Reg. No. 2955-9] One tablet weighing 0.28 grams to 140 ml of milk sample; preservation for Babcock laboratory test.

### B. Substitute compounds

Potassium dichromate (65.9%): [Ref. Reg. No. 2955-21] 1 tablet weighing 0.23 grams added to 180 ml milk provides preservation for 3 weeks.

### C. Comparative effectiveness and impact

(1) Substitute compounds cannot preserve milk samples as long as mercurial.

(2) Substitute chemical is satisfactory.

(3) Impact on industry expected to be minimal; consumer impact may call for increased cost.

# CHAPTER 2

# ANALYTICAL METHODS FOR MERCURY

Probably the single most important cause of the sudden increase in apprehension over mercury in the environment has been the rapid strides made in analytical methods used to detect trace amounts of mercury and its compounds. It can now be found in hitherto unsuspected substrates.

II.A. **Colorimetric** — For years the classical method for determination of mercury was the AOAC dithizone spectrophotometric procedure (Horwitz, 1970). In this procedure the sample, for instance, grain or tissue, is digested with nitric and sulfuric acids under reflux. Even after the solution becomes clear, indicating complete destruction of most of the organic matter, some of the organic mercury may still be so bound that it will not complex with dithizone reagent. In such a case, the results would be low. Further, some mercury can be lost by volatilization or absorption on the glass container.

Then, too, copper, gold, silver, palladium and platinum in trace amounts interfere giving high results. In the same manner, lead, zinc, nickel, and cobalt in larger amounts cause high results. The mercury dithizone complex is not stable to light and breaks down readily giving low results.

However, within the limits of its sensitivity and problems of interference, the dithizone method is satisfactory. A description of the method follows:

A sample equivalent to not more than 10 g dry weight is digested with $HNO_3$ and $H_2SO_4$ under reflux in a special apparatus designed to prevent loss of Hg by volatilization. The mercury is extracted from the digest with a chloroform solution of dithizone and is then separated from copper as a mercury thiosulfate complex. The complex is decomposed and the mercury again taken up in a chloroform solution of dithizone. The absorbance of the dithizone solution is measured at 490 nm and the mercury determined by comparison with the absorbance of standards. As little as $3 \mu g$ of Hg may be determined. For a dry produce such as grain using a 10-g sample, 3 g would be equivalent to a sensitivity of 0.3 ppm. With fish and other high moisture products a larger sample could be used. Assuming the use of a 20-g sample, the sensitivity of the method would be better than 0.2 ppm.

The method has little value in studying cases of mercury poisoning because of the larger amount of sample needed, the low limit of sensitivity and the many interferences.

Reviews of the methods for colorimetric analysis are given by Sandell (1959) and by Snell & Snell (1949).

II.B. **Atomic Absorption** — Even the advent of atomic absorption spectrophotometry did not immediately result in improvement in mercury analysis as mercury is one of the least sensitive of the metals to this method. However, a number of modifications of classical atomic absorption analysis permit greater sensitivity, reproducibility and ease of analysis. Some of these developments are as follows:

Jacobs and Goldwater (1960) digested samples of apples with permanganate, extracted the mercury with a chloroform solution of dithizone, evaporated, off the $CHCl_3$, volatized the mercury by heating the dry dithizone residue, swept the mercury vapor through a quartz windowed cell in a modified

Kruger mercury vapor meter and determined the mercury content by its absorbance. Values as low as 0.01 ppm Hg were reported.

Pappas and Rosenberg (1966) used a Schoniger combustion flask to burn samples. The released mercury was absorbed in dilute HCl and collected on a CdS-impregnated asbestos pad. The pad was pyrolyzed at 650°C and the released Hg vapor swept into a quartz-windowed cell where its absorbance was measured by a photometer using a mercury lamp as the light source. Sensitivity of 0.01 ppm Hg was reported for wheat samples.

Lidums and Ulfvarson (1968) burnt small samples (20-200 mg) of biological material in a stream of oxygen, and collected the Hg on gold foil. The gold foil was then heated, releasing mercury vapor which was swept into a cell and its absorbance measured by a photocell using a mercury lamp as the light source. As little as 0.001 $\mu$ g Hg/g sample could be determined. The procedure was said to work well for blood, plasma, urine and sea bottom sediments, but the authors were not quite satisfied with it for more difficult organic samples.

A.O. Rathje (1969) determined mercury in urine without digestion. The urine (2 ml) was treated with 5 ml conc. $HNO_3$, diluted to 50 ml and the mercury reduced by the addition of stannous chloride. Air or nitrogen was then bubbled through the solution and the mercury vapor swept through a drying tube into the cell of the detector. The instrument used was a Perkin Elmer Model 303 atomic absorption spectrophotometer with a GE 64811 mercury discharge lamp to provide the 253.7-mm line and with the burner assembly removed and replaced by an 8-inch cell with quartz windows. As little as 6 ng Hg could be detected, thus for a 2-ml sample indicating a sensitivity of 0.003 ppm.

Uthe, Armstrong and Stainton (1970) of the Fisheries Research Board of Canada determined mercury in fish using very small samples (0.1-0.5 g). The sample was first digested with $H_2SO_4$ at 50°-60°C and then with $KMnO_4$ at room temperature. The mercury was reduced with stannous sulfate and the mercury vapor swept by an air stream through a drying tube and a gas cell in a Perkin-Elmer atomic absorption spectrophotometer.

More recently the Association of Official Analytical Chemists has accepted the prescribed atomic absorption method as official. A brief description of the method is as follows:

Five gram samples of fish are digested under a water condenser first with $H_2SO_4$, $HNO_3$ and $NaMoO_4$ and then with $HNO_3$ and $HC10_4$. The digest is made up to 100 ml, and a 25-ml aliquot taken for atomic absorption analysis. Using a closed system consisting of a reaction flask, a drying flask, a gas cell in an atomic absorption spectrophotometer and a recirculating air pump, the mercury is reduced with stannous chloride and the resulting mercury vapors swept through the gas cell where the absorbance is measured.

II.C. **Neutron Activation** — The use of neutron activation analysis has excited the attention of many analysts, because of certain apparent advantages. It purports to be a nondestructive method. Also, it can yield definitive results with very small samples of even such materials as skin or hair. Further, in a reactor designed for automatic analysis, practically the entire operation becomes automatic including irradiation, counting and calculations.

However, the accuracy of the method is affected by the fact that sodium is present in practically all biological samples. If the level of sodium activity following irradiation is permitted to decay to tolerable limits, often the mercury has decayed to the point that it cannot be measured against the interference background.

The method of getting around this problem is to irradiate the sample and then add a few milligrams of carrier mercury, generally mercuric chloride. The sample is then digested, the mercury precipitated or extracted and the analysis completed by counting the isolated portion and calculating the mercury content from the radioactivity remaining.

However, that is unsatisfactory with many biological samples such as fish in which most of the mercury is present as methylmercury compounds. The mercury becomes radioactive on irradiation, but in the isolation step, much of the radioactive mercury is lost because of the difficulty in digestion. It simply is not precipitated or extracted with the carrier. Results may reflect only 10% of the actual level in such cases.

Sjostrand (1964) described the procedure used in Sweden. The sample, sealed in a quartz tube, was exposed to neutron radiation in a nuclear reactor. The sample was then transferred to a flask and 20 mg of Hg ($HgCl_2$) added as carrier and digested. The mercury was distilled from a perchloric acid solution and electrolytically plated out on a weighed gold foil. The foil was weighed to determine percent recovery of Hg and the $^{197}Hg$ measured by $\gamma$-spectrometry. Sensitivity of the procedure is said to be about $10^{-5}$ ppm Hg.

II.D. **Gas-Liquid Chromatography** — Since alkylmercury compounds tend to be difficult to analyze and yet are prevalent in many substrates, a number of scientists have attempted to devise methods suitable for samples containing such mercury derivatives.

K. Sumino (1968) used gas chromatography to determine methylmercury in marine products and phenylmercury in rice to levels lower than 0.01 ppm.

Westöö (1967, 1968) used electron capture GLC to determine methylmercury in fish and other foods of animal origin. She reported that most of the mercury present in fish, eggs and meat was in the form of methylmercury, 82% for ocean fish and 92% in fresh water fish.

In contrast to the two above methods in which the organic mercurials were chromatographed as the chlorides, Tatton and Wagstaffe (1969) extracted and chromatographed these compounds as their dithizonates. Apparently the intact dithizonates chromatographed and the specific organic mercurials could be identified by their retention time. Both these authors and Westöö also used TLC as an additional means of identification.

II.E. **Miscellaneous Methods** — Tong, Gutenman and Lisk (1969) applied the use of spark source mass spectrometry to analysis of apples for mercury. In this, a pair of indium electrodes was used to make a graded series of exposures on the same photographic plate for emulsion calibration relating microdensitometric measurements of mass line optical transmittance (%T) to exposure level (E). The %T values for silver (m/e 107), mercury (m/e 198, 199, 201, and 202), and their corresponding backgrounds were measured. These values were converted into E values according to the emulsion calibration curve. The ratio of mercury to silver was then determined by the exposure (E) ratio of mercury to silver (each element having been corrected for the isotopic abundance and background) according to Equation 1.

$$\text{mercury/silver (mole ratio)} = \frac{(E_{\text{mercury}} - E_{\text{mercury background}})\,A_{\text{silver}}}{(E_{\text{silver}} - E_{\text{silver background}})\,A_{\text{mercury}}} \quad (1)$$

where A mercury and A silver are the isotopic abundances of the respective lines of interest.

Mtusiak and coworkers (1964) described a method for analysis of mercury in biological substances wherein they passed wet digests or urine over copper powder over a period of 1 hour using suction to control the flow rate. The copper powder was then placed in the crater of the electrode of a spectrograph and the 2537 - A mercury line used for analysis.

Pakter (1968) describes a method he developed for determination of mercury in or by absorption on manganese dioxide. The mercury can then be driven from the manganese dioxide by heat and measured by conventional methods such as dithizone or atomic absorption methods.

# CHAPTER 3

# PREVALENCE OF MERCURY IN THE ENVIRONMENT

Mercury is one of the elements which make up the earth. In its elemental state at the earth's surface, it is a silvery liquid metal, approximately 13 1/2 times as heavy as water. Mercury is the only metal which occurs in the liquid state at ordinary earth temperatures. Like other liquids, it vaporizes and condenses in a pattern determined by its own vapor pressure and the barometric pressure of the environment in which it exists. Mercury is absorbed and is bound tightly by a variety of materials such as plant fibers and soils. It reacts with a variety of inorganic and organic compounds to form simple and complex molecules ranging from cinnabar, a mercury sulfide and the most common ore mineral, to the metallo-organic complexes which are used in pesticides and which are now found as a contaminant in fish (Fleischer, *et al.*, 1970). At this point in time, it is difficult to separate the "natural" background levels of mercury from those which are man-made. Certainly, a portion of the mercury found in water, soil, plants, and animals arises from "natural" sources. In areas where mercury pollution is known to occur from sources such as agricultural runoff, industrial wastes, and mining operations, increases above the "natural" levels can be expected. There remains, however, the question of just how much of the remaining background is due to the combustion of paper products and fossil fuels, the smelting of ores, weathering of paints, and other activities of man.

III.A. **Minerals and Rocks** — Cinnabar is the most commonly found mercury-bearing mineral. It contains 86% mercury by weight. Cinnabar is generally found in mineral veins or fractures, as impregnations, or having replaced quartz, in rocks near recent volcanic or hot-spring areas. The mercury content of broad categories of rocks in the earth's crust range from 10 to 20,000 ppb. Less than 20% of recorded rock samples have more than 1,000 ppb. Igneous rocks are the basic sources of mercury. These contain less than 200 ppb of mercury and average about 100 ppb. The mercury content of soils averages about 100 ppb and varies within relatively narrow limits. The background concentration of soils in California are 20 to 40 ppb. The Franciscan Formation of California, in which most of the State's mercury mines are located, has background levels of 100 to 200 ppb; anomalies in soils around these mercury deposits are in the range of 10,000 to 100,000 ppb (Fleischer, *et al.*, 1970).

III.B. **Atmosphere** — Because of the tendency of mercury to vaporize, it is distributed in the environment through aerial circulation. The atmosphere measured at ground level near mercury ore deposits may contain as much as 20,000 ng/m$^3$ of mercury. The concentrations over the ocean usually measure less than 1 ng/m$^3$. Land sources of airborne mercury apparently are subject to meteorological controls, i.e., mercury released into the air as a function of barometric pressure, time of day, and season. Rain serves to wash the mercury from the atmosphere. Immediately after a rainfall, mercury concentration in the air are negligible even near ore deposits (Wallace, *et al.*, 1971). The same author lists the air concentrations of mercury at various mineralized and nonmineralized areas of the United States in Table 1. Air over urban industrial areas contains mercury levels higher than background, and several measurements have indicated average values of 0.01 (Chicago, Ill.), 0.10 (Cincinnati, Ohio), and 0.17 (Charleston, W. Va.) $\mu$g/m$^3$. Concentrations of 1 to 14 $\mu$g/m$^3$ have been cited for New York City. Air concen-

Table 1. Maximum mercury concentration in air measured at scattered mineralized and nonmineralized areas of the western United States*

| Sample location | Maximum Hg concentration ($\mu g/m^3$)[1] Ground surface | 400 feet above ground[2] |
|---|---|---|
| **Mercury mines** | | |
| Ord mine, Mazatzal Mtns., Ariz. | 20.000 (50) | 0.108 (4) |
| Silver Cloud Mine, Battle Mtn., Nev. | 2.000 (50) | 0.024 (8) |
| Dome Rock Mtns., Ariz. | 0.128 (6) | 0.057 (20) |
| **Base and precious metal mines** | | |
| Cerro Colorado Mtns., Ariz. | 1.500 (5) | 0.024 (2) |
| Cortez gold mine, Crescent Valley, Nev. | 0.180 (60) | 0.055 (4) |
| Coeur d'Alene mining district, Wallace, Idaho | 0.068 (40) | |
| San Xavier, Ariz. | | 0.025 (3) |
| **Porphyry copper mines** | | |
| Silver Bell mine, Ariz. | | 0.053 (3) |
| Esperanza mine, Ariz. | | 0.032 (3) |
| Vekol Mtns., Ariz. | | 0.032 (4) |
| Ajo mine, Ariz. | | 0.030 (3) |
| Mission mine, Ariz. | | 0.024 (3) |
| Twin Buttes mine, Ariz. | 0.020 | 0.022 (3) |
| Pima mine, Ariz. | | 0.013 (3) |
| Safford, Ariz. | | 0.007 (2) |
| **Unmineralized areas** | | |
| Blythe, Calif. | | 0.009 (20) |
| Gila Bend, Calif. | | 0.004 (2) |
| Salton Sea, Calif. | | 0.004 (2) |
| Arivaca, Ariz. | | 0.003 (2) |

[1] Number of measurements shown in parentheses.

[2] Samples taken from single-engine aircraft.

*From Wallace, *et al.*, 1971.

trations of 100 $\mu g/m^3$ or larger have been reported within industrial buildings (Wallace, *et al.*, 1971).

III.C. **Water** — Contact of water with soil and rock during storm runoff, percolation into the ground, and movements underground where different geochemical stresses prevail, results in a natural distribution of mercury in water. Surface waters, except where they are influenced by special geologic conditions, or more recently by man-made pollution, generally contain less than 0.1 ppb mercury. This reflects the relatively low concentration of mercury in rain water and the relatively tight binding of mercury in organic and inorganic materials over which the water passes in its travel through the environment. A recent reconnaissance of river waters in 31 states showed that 65% of the samples tested were below 0.1 ppb, 15% exceeded 1.0 ppb, and only 3% were more than 5.0 ppb - the maximum considered safe for drinking water (Fleischer, *et al.*, 1970).

Because of mercury's tendency to sorb readily on a variety of earth materials, particulate matter suspended in water and bottom sediments of streams are more likely to contain high concentrations of mercury than the water itself. The best estimate is that suspended matter may contain from 5 to 25 times as much mercury as the water around it in areas of industrial pollution (Fleischer, *et al.*, 1970).

Sea water contains from 0.03 to 2.0 ppb mercury, depending on area, depth, and analytical procedures. Mercury concentrations increase from surface values of 0.10 ppb to 0.15 - 0.27 ppb at greater depths. The depletion of mercury in surface waters is attributed to its uptake by plankton and subsequent conveyance to depths by the biological activities of the marine food web (Wallace, *et al.*, 1971).

In the United States, the range of mercury levels in rivers is from less than 0.1 ppb to 6.0 ppb. Wallace, *et al.*, 1971 give a table of mercury content of selected rivers in the United States in 1970. In Minamata Bay, Japan, the values of mercury in water averaged from 1.6 to 3.6 ppb. Oceanic mercury is generally present as an anionic complex ($HgCl_4^{2-}$) which does not have a pronounced tendency to bind to particulate substances and subsequently settle out as do mercury compounds in freshwater situations (Wallace, *et al.*, 1971).

III.D. **Plants** — Terrestrial plants, like aquatic organisms, absorb minor elements, including mercury, from the soils in which they grow at rates depending on the quality of the environment and the genetic characteristics of the plants. Unlike aquatic organisms, there seems to be little tendency for terrestrial plants to concentrate mercury above environmental levels. Typical soils contain from 30 to 500 ppb mercury, and most of the plants which grow in them are likely to contain less than 500 ppb. When soil concentrations of mercury are extremely high (40,000 ppb) in the vicinity of cinnabar deposits, plants growing in them actually are likely to have mercury contents far below the level of their environment, for example, 1000 to 3000 ppb. Even in these instances, it is primarily the plants which are rooted through the surface soil into the mercury ore which have high mercury contents (Fleischer, *et al.*, 1970).

Smart (1968) reported results of studies carried out by various workers in the field which indicated translocation of mercury to fruit, tuber or seed following the foliar application of mercury fungicides. For example, tomatoes from untreated plants contain 0.01 ppm mercury, while tomatoes from plants which have been treated with mercurial fungicides contain 0.10 ppm.

Lindberg (1961) has also reported on the translocation of mercury from the leaves to the grain in plants which have had foliar treatment with phenylmercuric acetate. The translocation of mercury from treated seed to harvested grain is small. Westermark *et al.*, (1966), found 0.01 ppb mercury in grain grown from treated wheat seed containing 15 ppm mercury. Lagerwerff of the United States Department of Agriculture, in cooperation with Emry of the Oak Ridge National Laboratory and with analytical chemists of the National Bureau of Standards, demonstrated that leaves of corn plants grown from seed treated with ethylmercury-o-sulfonanilide, contained 0.14 ppm mercury (Mercurial Pesticide Review Panel Report).

It is known that plants take up and concentrate mercury from the soil or water to a variable extent. Marine algae, for example, have been found to contain from 0.023 to 0.037 ppm mercury. This is several hundred times the accepted concentration of mercury in sea water. Trees and shrubs growing near known cinnabar veins contain up to 3.5 ppm mercury. Rice from paddies treated with mercurial pesticides have higher mercury content, e.g., Japanese rice versus rice from other countries. However, Yamada (1970) treated rice with $^{203}$Hg-treated phenylmercuric acetate and failed to grow rice with a higher mercury content than the "normal" background. Again, on the other side of the coin. Wallace, *et al.*, report on the work of Furutani and Osajima which gave positive results. They demonstrated that a well-drained soil containing 0.3 ppm mercury grew rice containing 0.3 ppm, while a poorly drained soil containing 1.4 ppm yielded rice containing 0.8 ppm mercury.

Evidence is in favor of the translocation of mercury from soil to plants, including the edible portions. In addition, evidence is also in favor of the conclusion that mercury-treated plants will bear fruit with a higher mercury content than the normal background.

III.E. **Animals** — "Background" levels of mercury for animals are difficult to assess, since the agricultural use of mercury products is so widespread, and completely uncontaminated food sources are rare. Wallace, *et al.*, (1971), give the normal value for eggs and the flesh of birds and animals as generally less than 0.02 ppm. Marine fish have mercury concentrations usually below 0.10 ppm and nearly always below 0.15 ppm, whereas the mercury levels of 0.20 ppm or less are assumed to be normal for fresh water fish. The higher background levels found for fish when compared to other animals or fruits and vegetables is due to the marked ability of fish to accumulate mercury.

III.F. **Fossil Fuels** — From the beginning of time, the products and residues of geochemical processes and the life cycles of terrestrial and aquatic organisms have combined to yield very appreciable mercury contents and distinct regional patterns in fossil fuel deposits. Joensuu (1971) analyzed 36 American coals and found an average mercury content of 3.3 ppm.

Applying a conservative estimate of 1 ppm mercury in coal to the yearly world production of coal of 3 x $10^9$ tons per year. Joensuu concluded that 3000 tons of mercury per year are released into the environment. He compares this to the calculated upper limit of natural release of mercury due to chemical weathering of 230 tons per year.

III.G. **Other Sources** — Other sources of mercury in the environment have included mine tailings, discharges from chlor-alkali plants, and dissipative uses such as paints, agricultural pesticides, pulp and paper, and pharmaceuticals. Of the dissipative uses, paint and agricultural pesticides are the largest. Mercury losses from chlor-alkali plants have been greatly reduced in the past year, and the pulp and paper uses have been curtailed.

# CHAPTER 4

# PHARMACOLOGY OF MERCURY

The basic pharmacological activity of mercury is centered about the strong attraction of this metal for certain sensitive ligands of proteins located in enzymes, cell membranes, and cell stroma. The total body response to this binding is dependent upon the cells, tissues, and enzyme systems affected and the concentration of mercury present in these sites. Therefore, the degree of absorption and excretion and the tissue distribution play a major role in the final effect of mercury on the organism. The different forms of mercury vary in their absorption, distribution, and excretion characteristics and, therefore, vary in their effects upon man or animal.

## IV.A. **Absorption**

The absorption of mercury and its compounds varies considerably with the chemical form of the metal and with the route of exposure.

IV. A. 1. *Oral Absorption* — It is generally considered that elemental mercury is not absorbed from the intestinal tract. The mild catharsis, diuresis, or intoxication resulting from the ingestion of mercury results from small particles of oxides or sulfides found on the surface of mercury. These oxides and sulfides are the result of atmospheric exposure and oxidation. In water, especially in the presence of the chloride ion, mercury can be slowly oxidized to the mercuric ion. So long as the state of subdivision of the mercury is quite coarse, the rate of solution in body fluids is too slow to give rise to cumulative effects (Goodman and Gilman, 1965).

Soluble inorganic mercurials, such as mercuric chloride, are absorbed from the gastrointestinal tract but only to the extent of about 2% (Clarkson, 1971). This is probably because these compounds show a strong avidity for a large number of groupings on proteins, and after binding to SH groups, the mercuric ion still contains a free valence capable of combining with some other properly placed group. This fixes the mercuric ion to the protein of the intestinal mucosa preventing or delaying absorption, and producing local irritation (Hughes, 1957).

Swensson, Lundgren and Lindstrom (1959) studied the absorption of mercuric chloride and mercuric nitrate from subacute oral administration in rats. The animals were administered the compounds in water, fed *ad libitum*, at a concentration of 2 mg Hg/liter of water. The animals were sacrificed at 1, 2, and 3 weeks. Absorption of both mercurial salts occurred as indicated by very low levels of mercury in the blood, brain, and liver as compared to organic mercurials.

Fitzhugh, Nelson, Laug, and Kunze (1950) studied the absorption of mercuric acetate and phenylmercuric acetate from chronic oral administration in rats. The animals were administered the compounds in their diets at levels ranging from 0.1 to 160 ppm, *ad libitum*, for up to 2 years. Feces and urine samples were analyzed for mercury at 6 months and 1 year. The livers and kidneys were analyzed for mercury in animals sacrificed at 1 year and at termination. Diets containing the same quantity of mercury but in different forms, viz., phenylmercuric acetate and mercuric acetate, produced a large difference in tissue concentration of mercury. For example, at a dosage level of 0.5 ppm mercury, the liver contained, on the average, 2 1/2 times and the kidneys 28 times as much mercury after administration of phenylmercuric acetate as after mercuric acetate. On the whole, there was a significant positive regression for both compounds relating dosage level with storage. Forty-three percent of the mercury ingested as mercuric acetate appeared in the feces, whereas only 20 percent of mercury ingested as phenylmercuric acetate appeared in the feces. This figure is not in agreement with Clarkson who found only 2% absorption of mercuric chloride by the oral route. One possible explanation for the low fecal excretion of mercury after mercuric acetate ingestion is that of Hughes cited above. The bivalency of the mercuric ion causes it to link protein of the intestinal mucosa, becoming fixed and thus limiting its absorption and also excretion in the feces. However no firm conclusions may be drawn from fecal excretion, since Ulfvarson (1962) has shown that a significant proportion of absorbed mercury is excreted by the fecal route.

In the study of Swensson, Lundgren, and Lindstrom, cited above, phenylmercuric acetate, an arylmercury compound, was absorbed to a much greater extent than either mercuric chloride or mercuric nitrate as indicated by blood levels of mercury. Much higher levels were also reached in the brain, kidney, and liver. These findings are in agreement with Fitzhugh, *et al.* (1950). Ulfvarson (1962) also found much higher levels of mercury in blood plasma, brain, liver, and kidneys in rats dosed with phenylmercuric acetate than those dosed with mercuric nitrate.

The absorption after oral administration appears to be much greater for the alkylmercury compounds than for either inorganic mercury or arylmercury compounds. Swensson, *et al.* (1959) found much higher levels of mercury in the tissues of animals fed methylmercuric hydroxide or cyano (methylmercuric) guanidine than in the tissues of animals fed mercuric chloride. Ulfvarson (1962) found that methylmercuric cyanide, methylmercuric hydroxide, and methylmercuric propandiolmercaptide were absorbed to about the same extent *via* the oral route. In reviewing the available data on both man and the rat, Berglund and Berlin (1969) concluded that the intestinal absorption of methylmercury is more than 90%.

Clarkson (1971) studied the rate of absorption of inorganic and methylmercury compounds, labelled with $^{203}$ Hg in food by whole-body counting techniques. The experimental results indicated that when mercuric chloride was added to food, absorption across the gastrointestinal tract was small, averaging less than 2% of the daily intake. When the total body burden of mercury was plotted against the time on diet, in days, the curve showed a sharp rise within the first day of administration of radioactive food and a sharp fall after the animals were returned to normal food. The sharp rise and fall were equal in magnitude and corresponded to approximately 25% of the daily intake. Such curves are typical of isotopes that are poorly absorbed by the gastrointestinal tract. The rapid rise and fall correspond to the effect on whole-body count of the isotope's entry into and removal from the gastrointestinal tract, respectively. The curve also exhibits a slowly rising phase during the remainder of the times the animals are fed radioactive food. The slope of the curve corresponds to the daily net absorption of the isotope into the blood stream and body tissues. When radioactive methylmercury chloride was fed in the diets of the animals, the curve describing the whole-body counts was entirely different from those above. The whole-body count rose continuously throughout the period of exposure. The curves suggest that the absorption of methylmercury from food is practically complete.

Clarkson's data are difficult to reconcile with the data of Fitzhugh, *et al.* and with the high acute oral toxicity of the inorganic mercurials as compared with the organic mercurials.

IV.A.2. *Absorption through the Lungs* — Metallic mercury and all of its compounds are absorbed in the lungs. The organomercurials vary in their volatility and, therefore, differ in their hazards *via* the inhalation route. The following table of the saturated vapor concentrations of organic mercurial compounds and of metallic mercury comes from Swensson and Ulfvarson (1963).

**Saturated Vapor Concentration of Some Mercurial Fungicides at 20°C**

| Organomercury Cation | Anion | Saturated Vapor Conc. $\mu g/M^3$ |
|---|---|---|
| methylmercury | chloride | 94,000 |
| " | bromide | 94,000 |
| " | iodide | 90,000 |
| " | acetate | 75,000 |
| " | hydroxide | 10,000 |
| " | toluenesulfonate | 15,000 |
| " | benzoate | 2,000 |
| " | dicyandiamide | 300 |
| ethyl mercury | chloride | 8,000 |
| " | bromide | 7,000 |
| " | iodide | 9,000 |
| " | dicyandiamide | 400 |
| " | monohydrophosphate | 50 |
| methoxyethylmercury | chloride | 2,600 |
| " | acetate | 2 |
| phenylmercury | acetate | 17 |
| " | chloride | 5 |
| " | nitrate | 1 |
| " | methanedinaphthyldisulfonate | 2 |
| metallic mercury | | 14,000 |

In a study in which mice were exposed to a vapor stream of air containing various organomercurials, Swensson (1952) found the chlorides were more toxic than the dicyanamides of alkylmercury compounds. This is in agreement with the lower vapor pressure of the latter. Gage (1961) has shown in his experiments in which rats were exposed to an atmosphere containing 1 mg of mercury per cubic meter of air for varying periods, that absorption is rapid and complete and the turnover in all tissues, except the brain, is rapid; most of the mercury is removed within a week after exposure has ceased.

In a study designed to measure the absorption, distribution, and excretion of inhaled mercury vapor, female rats were exposed 24 hours per day for 28 days to a concentration of 1 mg $Hg/M^3$ of air. The rats survived but lost weight, became lethargic, and showed slight tremors, especially when lifted by their tails.

A second series of rats were given repeated continuous exposures to the same concentration of mercury vapor for 100 hours from Monday through Friday in each week for six weeks. As a result, growth was retarded, the rats appeared lethargic and squeaked when touched, and after 5 weeks these rats also showed fine tremors when lifted by their tails.

In a third series of experiments, rats were exposed to the same mercury vapor concentration for 7 hours per day for 5 days per week for 18 successive weeks. The resulting symptoms were similar to those in the first and second experiments but appeared more slowly, the only difference being that the rats showed a slight increase in weight during the experiment.

The author calculates that if the results obtained in rats in these experiments with mercury vapor at 1 mg Hg/M$^3$ can be applied to a man breathing 10 M$^3$/day for 5 days with the maximum allowable concentration of mercury vapor of 0.1 mg/m$^3$, then the daily absorption might be expected to be about 500 $\mu$ g, with a total excretion over 7 days of approximately 2.5 mg. If the total exposure were short, the bulk of the mercury would be eliminated in a few days, but if the exposure continued for several weeks, the resulting accumulation of mercury would be excreted for a considerable time and could amount to several hundred micrograms per day (Gage, 1961).

Kosmider (1965) studied the pathogenetic mechanisms of poisoning in rabbits resulting from the inhalation of mercury vapors. In these experiments, rabbits were exposed to mercury vapor concentrations of 10.6 mg/m$^3$ for 1 to 5 hours daily for 30 days. This exposure resulted in the alteration of function of a number of enzymes and damage to several organs.

IV.A.3. *Absorption through the Skin* — All forms of mercury may be absorbed through the intact skin. Laug, *et al.* (1947 a,b,c) studied the dermal absorption in rats and rabbits of several of the official mercurial ointments. The preparations studied were Mild Mercurous Chloride Ointment, NF (Calomel Ointment) which contains 30% HgC1; Strong Mercurial Ointment, NF (Mercurial Ointment) which contains 50% Hg; Mild Mercurial Ointment, NF (Blue Ointment) which contains 10% Hg; and Ointment of Oleated Mercury, USP which contains 23% Hg. Both Strong Mercurial Ointment, NF and Mild Mercurial Ointment, NF contain finely divided metallic Hg. A small amount (5%) of mercuric oleate is added to the mercury in the preparation of the ointment to form a film over the globules of mercury to facilitate the dispersion in the ointment.

It was determined that dermal absorption of mercury was proportional to (1) the duration of contact, and (2) the area of skin exposed. The mercury content of the kidneys of rats after 24 hours continuous skin contact to 8% of the body surface with 0.4 g of Mild Mercurous Chloride Ointment, NF was about 90-fold that found in the controls (27.2 $\mu$ g Hg versus 0.3 $\mu$ g Hg/g wet kidney) and about 130-fold after 48 hours contact. In this experiment, mercury levels in rat liver increased by 10- to 20-fold (0.8 $\mu$ g at 48 hours versus 0.06 $\mu$ g/g wet liver of controls). The greatest absorption occurred with Ointment of Oleated Mercury, which gave 30.1 $\mu$ g/g wet tissue.

The vehicle in which mercury is suspended and the particle size of mercury have an influence on the dermal absorption. However, the concentration of mercury in the test ointments appeared to have little influence on total mercury absorbed. The kidney concentrations of mercury after application of Mild Mercurial Ointment and Strong Mercurial Ointment were almost identical.

Recent studies in humans conducted by the Food and Drug Administration with a 1% ammoniated mercury bleach cream to which 3% $^{203}$Hg had been added, showed that an average of 2.4 $\mu$ g/cm$^2$ mercury penetrated intact skin in a 24-hour period (unpublished data). The author extrapolates these results to application of this type of product to a 10- by 15-cm area on each hand or arm (300 $cm^2$ total skin area) from which a theoretical 720 $\mu$ g mercury could penetrate skin in a 24-hour day. According to these studies, the urinary excretion rate may be as little as 4% in 5 days, indicating a possible problem of heavy metal poisoning from skin absorption. Cases of nephrotic syndrome in humans from topical use of ammoniated mercury have been reported (Becker, 1962; Silverbert, *et al.*, 1967).

Mercury is absorbed slowly through intact skin and much more rapidly through broken skin. The mucosa offers little resistance to penetration of mercury. Instillation of 0.1 ml of a 0.05% solution of phenylmercuric acetate into the vaginal tracts of rats (9 $\mu$ g/kg) resulted in about 28% residue of mercury in the kidney and liver combined immediately following a 24-hour exposure.

### IV.B. **Distribution**

The distribution of mercury in the organs and tissues of animals after absorption varies with the form in which the mercury is administered and with the species of the animal studied. Mercury derived from inorganic and aryl compounds appears to accumulate in the liver and kidneys, whereas mercury derived from alkyl compounds is more evenly distributed throughout the body. There are considerable species differences in the distribution patterns of mercury among different mammalian species — most pronounced is the low brain content of mercury in the rat as compared with other species after the administration of alkylmercury compounds.

IV.B.1. *Blood* — The distribution of mercury in the blood between the red blood cells and the plasma is dependent upon the type of mercury administered. There appear to be significant differences between the red blood cell/plasma distribution characteristics of metallic mercury, inorganic mercury, arylmercury, and alkylmercury. Some species variations have been noted.

Metallic mercury, inhaled as mercury vapor, results in a higher concentration of mercury in the red blood cells than in the plasma. After inhalation of mercury vapors, 67% of the mercury in monkeys' blood and 84% of the mercury in rabbits' blood was bound to the red blood cells (Berlin, 1969).

Inorganic mercury accumulates in the plasma of the blood. This has been demonstrated after oral administration to rats and intravenous administration to rats, rabbits, and dogs by Swensson, *et al.* (1959a; 1959b). In rabbits and monkeys injected with inorganic mercury, the red blood cell level was approximately 25% of the blood mercury level (Berlin, 1969). Inorganic mercury reacting with the red blood cells binds to hemoglobin, not only with the sulfhydryl groups but also with the imidazole residues (Resnik, 1964).

Mercury derived from arylmercury compounds is bound to the red blood cells to a greater extent than is mercury derived from inorganic compounds. Berlin (1969) states it is evenly distributed between the plasma and the red cells, while Swensson (1959a, 1959b) states that phenylmercury compounds are bound mainly to the red blood cells. In either case, it appears to be intermediate between inorganic mercury and alkylmercury.

Mercury derived from alkylmercury compounds is bound mainly to the red blood cells (Swensson, *et al.*, 1959a, 1959b). Burgland and Berlin (1969) reported that, in all species studied, 90% of the methylmercury in the blood is bound to the red blood cells. The fraction in the plasma varies with the species; in man 10%, in the rat 4.5%, in the rabbit 10%, and in the squirrel monkey 9%. Takeda (1968a) found that, of the alkylmercury compounds studied (methylmercuric chloride, ethylmercuric chloride, and n-butylmercuric chloride), there was a marked accumulation of alkylmercury in the blood, especially in the nonstromal fractions of the erythocytes. Ethylmercuric chloride gave lower concentrations in the blood than did n-butylchloride. In a later study, Takeda (1968b) found that more than 97% of the mercury in the blood after the administration of $^{203}$Hg-labeled ethylmercuric chloride was in the form of ethylmercury. The ethylmercury residues accumulated in the hemoglobin, forming a mercaptide linkage with SH groups of cysteine residues in the hemoglobin molecules. He attributes the high, long-lasting accumulation of aklylmercury in the blood to the high affinity of alkylmercury for hemoglobin.

Phenylmercuric acetate appears to be absorbed unchanged, regardless of the route of administration. The transportation *via* the blood appears to be as phenylmercury. The phenylmercury present in the blood after 48 hours appears to account for the total mercury in the blood (Miller, *et al.*, 1960).

IV.B.2. *Brain* — The concentrations of mercury found in the brain after administration of inorganic, aryl, and alkylmercury compounds are lower than the concentrations found in other organs and tissues. While the blood-brain barrier is a relative hindrance to their passage, the alkylmercury compounds reach a higher concentration in the brain than do the arylmercury compounds. However, there is some disagreement in the literature as to these differences, especially in the rat. In addition, there are considerable species differences in mercury levels in the brain. In the rat, short-chain alkylmercury compounds reach a higher level in the brain than do the longer chain compounds.

Swensson, *et al.*, (1959a) administered $^{203}$Hg-labeled mercuric chloride, mercuric nitrate, phenylmercuric acetate, cyano (methylmercuri) guanidine, and methylmercuric hydroxide to rats in their drinking water at 2 mg Hg per liter for 3 weeks and determined the distribution of mercury in the various organs. He found that the inorganic compounds gave a very low mercury content in the brain: In fact, no mercury could be demonstrated after 1 week exposure and very little after 2 or 3 weeks. The animals which received phenylmercuric acetate had somewhat higher mercury contents in the brain, and the animals exposed to cyano (methylmercuri) guanidine had much higher levels. The ratio between blood and brain mercury contents seemed to be constant for each substance and indicated a distribution equilibrium. However, in an earlier study (1959b) Swensson failed to demonstrate these differences after a single intravenous administration of 100 $\mu$ g $^{203}$Hg as mercuric nitrates, phenylmercuric acetate, or methylmercuric hydroxide.

Friberg (1957) compared the tissue distribution of mercury in rabbits after the single subcutaneous administration of 2 mg $^{203}$Hg per kg. of body weight as mercuric chloride or phenylmercuric acetate. Readings were made after 1, 6, and 40 days. The readings in the cerebrum, cerebellum and brain stem were less than 1% of the corresponding renal levels. He found no significant difference in the mercury concentration in the brain resulting from the administration of mercuric chloride or phenylmercuric acetate.

Gage (1964) studied the distribution, metabolism and excretion of phenylmercuric acetate and methylmercuric dicyandiamide after repeated subcutaneous administration of 0.15 mg Hg per rat and after a single 0.5 mg dose.

More mercury accumulated in the brain with methylmercuric dicyandiamide than with phenylmercuric acetate. Gage postulated that the higher concentration of methylmercury in the brain was due to the sustained higher concentration in the plasma and not that methylmercury had a greater ease of penetration into the central nervous system.

Ulfvarson (1962) administered $^{203}$Hg-labeled mercuric nitrate, methylmercuric hydroxide, methylmercuric dicyandiamide, phenylmercuric hydroxide, and methoxyethylmercuric hydroxide subcutaneously to rats at a dosage level of 0.1 $\mu$ gm Hg per gram of body weight every other day. He analyzed the radioactivity in the tissues at 6, 16, and 18 days. He concluded that radioactivity found in the brain could be attributed to the blood content of this organ and that there is no reason to believe that alkyl compounds have a greater affinity for the brain.

In a series of experiments on the rabbit by Swensson *et al.* (1959b), intravenous injections of methylmercuric hydroxide were given at approximately 10 mg mercury per kilogram of body weight, corresponding to approximately the $LD_{50}$. He compared the brain concentrations of mercury resulting from this dose to the concentration in an earlier study in which only 1 mg mercury per kilogram of body weight was administered. The mercury contents of the organs agree closely with the amount injected, except the brain where the increase in the mercury content was much less than would be expected from the increase in dose.

Berlin, *et al.* (1965) demonstrated that, although the blood-brain barrier is a relative hindrance to methylmercury penetration, the diffusion of mercury into the brain can be accelerated by the simultaneous administration of dimercaprol (BAL).

Short-chain alkylmercury compounds may accumulate more in the brain than do the long-chain compounds. Takeda, *et al.* (1968) found that the brain/blood ratios for ethylmercury were higher than those for n-butylmercury. When ethylmercuric chloride was administered, the concentration of mercury in the brain was 2 to 3 times higher than in plasma, while the concentration in the brain was approximately equal to that in plasma when n-butylmercuric chloride was administered. Sebe, *et al.* (1962) studied the toxicity of a number of alkylmercury compounds. The alkyl compounds containing a R-Hg, or R-Hg-S radical, with a methyl, ethyl, or n-propyl chain administered orally to rats were toxic to the central nervous system and induced paralysis of the legs. Isopropylmercury compounds and other alkylmercury compounds with 4 to 5 carbon atoms were shown not to cause injuries to the nervous system. Suzuki, *et al.* (1963) studied the distribution of mercury in mice administered methyl, ethyl, or propylmercuric acetate. The highest concentration of mercury in the brain was obtained with ethylmercuric acetate. In addition, the mercury in the brain resulting from the administration of the ethylalkyl compound was more rapidly dissipated than that from the methyl or propyl derivatives. In a later study, Suzuki, *et al.* (1964) compared the distribution of mercury resulting from the administration of n-butyl, isobutyl, propyl, and amylmercuric acetates. The mercury concentration in the brain was lowest for the amyl compound. There was no marked difference in the uptake of mercury in the brain from the other acetates. However, when graded doses of the compounds were given, there was a very marked increase in mercury concentration in the brain in relation to dose for the n-propylmercuric acetate.

In three separate studies, Berlin, *et al.* (1963a, 1963b, 1963c) used an autoradiographic technique to differentiate the distribution of mercuric chloride, phenylmercuric acetate, and methylmercuric dicyandiamide.

With mercuric chloride, Berlin, *et al.* found that the brain takes up mercury slowly and retains it for a long time in comparison with other organs, but appreciable levels are accumulated only in parts which constitute a small fraction of the total brain tissue. They speculate that this may explain why previous investigators have been unable to find deposits of mercury in the brain adequate to explain the clinical picture; measurements were made on the whole organ or large parts of it and generally at relatively short times after administration. The localization of mercury in tissues adjacent to the cerebrospinal canal causes Berlin to suggest that mercury reaches the brain through the cerebrospinal fluid rather than the blood. There is a relatively high concentration of mercury in the gray matter of the cerebellum, area postrema, the subfornical body, and the tuber cinereum.

After phenylmercuric acetate, the picture is quite similar to that of mercuric chloride; the autoradiograms of the brain, brain stem, and spinal cord in the first 24 hours after exposure show a uniform density which is slight in comparison with the other organs. After 4 days, there is a more differential accumulation of mercury which is even greater at 16 days. As with inorganic mercury, there is an accumulation in the dorsal part of the brain stem, especially in the area corresponding to the area postrema, in areas adjacent to the lateral ventricle, and in the area corresponding to the hypothalamus and tuber cinereum. It also accumulated in the gray substance of the cerebellum.

After an injection of methylmercuric dicyandiamide, as with inorganic mercury and phenylmercury, very little mercury is taken up by the central nervous system in the first few hours. Accumulation occurs gradually over a period of several days and is not correlated with the level of mercury in the blood. The distribution in the brain is quite different from that seen after the injection of inorganic mercury or phenylmercury. With these compounds, the distribution was heterogeneous, but after methylmercury it is more uniform. Although the gray substances takes up more mercury than the white, as in the case of inorganic mercury, the regions which show the maximum concentration of mercury are not the same. These are the hippocampus and the gray matter of the cerebellum.

IV.B.3. *Liver, Kidney, and Other Organs and Tissues*— After absorption, the aryl and alkylmercury compounds accumulate at higher concentrations in the liver and kidneys than do the inorganic compounds of mercury. The alkylmercurys are more evenly distributed throughout the body than the other two groups of compounds. Inorganic and phenylmercury compounds translocate from the liver to the kidneys with time. The spleen and muscle concentrations of mercury are lower than those found in the liver and kidneys. Both aryl and alkylmercury compounds give a high content of mercury in the hair. With methylmercury, the concentration of mercury in the hair is greater than in the other tissues.

Swensson, *et al.* (1959a, 1959b) studied the distribution of mercury in the body of rats, rabbits, and dogs after the administration of inorganic, aryl, and alkylmercury compounds, both by the oral and intravenous routes. He found that administration of the organic compounds by the oral route in rats resulted in much higher mercury concentrations in the liver and kidneys than the inorganic compound.

On the other hand, after intravenous administration to rabbits, mercuric nitrate and phenylmercuric acetate were deposited chiefly in the kidneys, whereas methylmercuric hydroxide appeared to be more uniformly distributed throughout the body. Ellis, *et al.* (1967) studied the tissue distribution of mercury after single oral doses of $^{203}$Hg-labeled mercuric acetate or phenylmercuric acetate. With both compounds, the highest concentrations of mercury were found in the kidneys and then the liver, lung, and heart; accumulations in other organs were comparatively small. In the kidney and liver, subcellular distribution of the compounds was quite similar. Takeda, *et al.*, (1968), administered single subcutaneous doses of inorganic mercury, phenylmercury, ethylmercury, and n-butylmercury compounds. With the alkylmercury compounds, there was a gradual increase in the accumulation of mercury in the kidneys. There was a difference in the distribution of ethylmercury and n-butylmercury. With butylmercury, there was a larger amount of mercury in the blood than in the muscles. The opposite was true with ethylmercury.

Friberg, *et al.* (1957) studied the distribution of $^{203}$Hg-labeled mercuric chloride and phenylmercuric acetate in rabbits after a single subcutaneous injection. In the kidneys, almost all of the mercury was in the cortex. The mercury concentrated in the tubules and not in the glomeruli. Bergstrand, *et al.* (1958), administered $^{203}$Hg-labeled mercuric chloride and phenylmercuric acetate subcutaneously to rabbits at a dose of 2 mg per kilogram of body weight. The kidneys were studied 1 and 6 days after injection. Mercury invariably accumulated in the cortex and subcortical stratum of the kidneys. Much of the activity in the renal cortex was derived from the regions around the intralobular vein and the neighboring straight tubules. In the subcortical stratum, the activity could be traced to the tubular epithelium between the arciform veins. No activity was demonstrated in the glomeruli. In sections taken 6 days after injection of organic mercury, the activity in the subcortical stratum was even higher. Whether or not this is specific for organic mercury could not be definitely decided.

Organic mercurials reach a higher concentration in the kidneys than do the inorganic mercurial compounds (Swensson, *et al.*, 1959a, 1959b). In the kidneys, almost all of the mercury is found in the cortex. The mercury is concentrated in the tubules and not in the glomeruli (Friberg, *et al.*, 1957; Bergstrand, *et al.*, 1958). This localization of mercury in the renal cortex is to be expected, since this is the basis for the pharmacological action of the mercurial diuretics. Two mechanisms may contribute. In the first place, organic mercurials are weak acids which are secreted in the proximal region of the renal tubule. In the second place, the hemodynamics of the kidney are favorable to cortical deposition. The cortex is the first area of the kidneys with which mercury in the arterial blood will equilibrate. Moreover, since mercury is present in the blood as a nonultrafilterable protein-complex, it will be retained in the bloodstream during the glomerular filtration process. Consequently, the concentration of the mercurial in the bloodstream just distal to the glomerulus will be increased by 20%, depending upon the fraction of plasma filtered. In addition, the distribution of blood vessels in the medulla is such as to produce a low effective blood flow in the region of the loop of Henle and the distal tubule (Passow, *et al.*, 1961).

With inorganic mercury there is a marked concentration of mercury in the liver, in the periportal connective tissue, lymph space, or in the bile ducts. Organic mercury produces a more even distribution pattern, except for areas of slightly increased density around the portal vein. There is a higher concentration of mercury in the red pulp of the spleen than in the white pulp (Friberg, *et al.*, 1957).

The placenta apparently constitutes a barrier to mercury after the administration of mercuric chloride. In the 24-hour autoradiograms, it appears strongly darkened; the visceral yolk sac epithelium adjacent to the fetus shows only traces of mercury. Localization apparently corresponds to that of the maternal organs, as judged from the faint pictures (Bolin 1963a).

The placenta affords a barrier to mercury after the administration of phenylmercuric acetate as it does with mercuric chloride. While the placenta takes up a large amount of mercury, only traces are demonstrable in the fetus. After 8 to 16 days, however, the yolk sac epithelium and the fetal membranes show a greater amount than the placenta.

The placenta does not constitute a barrier to mercury after the administration of methylmercuric dicyandiamide. In the fetus, the concentration equals that in the mother, and the distribution differs only in that there appears to be more mercury in the fetal skin.

## IV.C. **Metabolism and Excretion**

Inorganic mercury and phenylmercury compounds may be slowly metabolized in the liver and kidneys, while alkyl and alkoxyalkylmercury compounds are relatively stable in the body. Ulfvarson (1962) studied the distribution and excretion of mercuric nitrate, phenylmercuric hydroxide, methoxyethylmercuric hydroxide, methylmercuric hydroxide, and methylmercuric dicyandiamide after subacute, subcutaneous administration to rats. He found that a simple distribution equilibrium between different organs existed for the alkyl and alkoxyalkylmercury compounds. This was not the case for mercuric nitrate or phenylmercuric hydroxide which were continuously translocated toward the kidneys. There is no reason to believe such a gradual accumulation should occur with stable substances which are able to pass permeable membranes. It is very likely that this translocation is connected with a chemical change of the compounds, which results in a gradual change of the partition coefficients. The chemical reactions to the final product must also be rather slow, since otherwise the new derivatives would immediately distribute in the final way. Ulfvarson estimated the half-life of the methylmercury salts as between 15 and 20 days and the methoxyethylmercury hydroxide as between 4 and 10 days. Since mercuric nitrate and phenylmercuric hydroxide were unstable in the body, the estimation of their half-life was more difficult. The excretion data indicate a half-life of between 4 and 10 days in the beginning of the experiment.

Berlin (1963) studied the renal uptake, excretion, and retention of mercury in rabbits during an infusion of phenylmercury acetate or methylmercuric dicyandiamide. The renal excretion did not exceed 10% of the amount of mercury in the blood passing through the kidneys in the case of either compound. There was no correlation between the amount of mercury accumulated in the kidneys and the urinary excretion of mercury, although there was a correlation between the urinary excretion of mercury and the blood concentration. In the case of phenylmercuric acetate, a small percentage of the infused mercury was excreted in the urine while about 30% was accumulated in the kidneys. After infusion with methylmercuric dicyandiamide, the urinary excretion of mercury did not exceed a few parts per thousand of the infused dose and less than 10% accumulated in the kidneys.

Miller, *et al.* (1960, 1961) administered phenylmercuric acetate and ethylmercuric chloride intravenously, intramuscularly, and orally to chicks, rats, and dogs. Phenylmercuric acetate appeared to be absorbed unchanged, regardless of the route of administration. In rats, slightly over half of the urinary mercury was in a form other than phenylmercuric acetate. Metabolism was fairly rapid and occurred mainly in the liver and kidney, with accumulation of mercury in these organs. With dogs, a greater proportion of the urinary mercury was not present as phenylmercury. Phenylmercuric acetate was detectable only for 96 hours. Less than 10% of the initial dose was excreted unchanged in the urine. In contrast, when ethylmercuric chloride was given to chicks and rats orally, the intact ethylmercury was detectable in the liver and kidneys for 21 days. The excretion of mercury in the urine of rats was not as rapid as that observed with phenylmercury, nor was there any appreciable excretion of the unchanged compound. However, total mercury levels in the kidneys showed a marked increase. In addition, the fecal excretion of mercury over a 7-day period following administration of ethylmercury was only one-twentieth of that observed in the phenylmercury study, suggesting the liver was not involved in the metabolism and excretion of ethylmercury. Chicks did not show accumulation of mercury in the kidneys following the administration of ethylmercury, and it appeared the liver was the major organ involved in detoxication. A comparison of the excretion of mercury in rats fed $^{203}$Hg-labeled phenylmercuric acetate or mercuric acetate showed that 68% of the activity from a single dose of phenylmercuric acetate accumulated in the feces, and 12.6% of the inorganic mercury was excreted in the feces and only 1 to 4% in the urine (Ellis and Fang, 1967).

Swensson, *et al.* (1959) studied the distribution and excretion of $^{203}$Hg-labeled mercuric nitrate, phenylmercuric acetate and methylmercuric hydroxide in rats and dogs. There was a continuous outflow of mercury from the various organs until 32 to 64 days after the initial injection when the organs were practically free from mercury. The kidney level of mercury fell very slowly after methylmercury. This was probably due to a continuous supply from other parts of the body that were being depleted of mercury. There were considerable differences between the rate of excretion of the three compounds. The mercury concentration was appreciably lower in the case of methylmercury than after mercuric nitrate or phenylmercury. The total excretion within 4 hours of injection was essentially lower for the methylmercury compound than for the other two. The methyl and phenyl compounds were excreted most rapidly at the beginning of the experiment when the concentration of mercury in the blood was highest, the rate decreasing with the fall in concentration of mercury in the blood was highest, the rate decreasing with the fall in concentration in the blood. After the injection of inorganic mercury, a high initial excretion was followed by a period of anuria, after which only traces of urine with a very high mercury content were excreted. The rate of urinary excretion was greater after phenylmercury than with methylmercury. Although, in both cases, there was a steady excretion of mercury which was related to the concentration in the blood. The anuria following mercuric nitrate administration suggests that this compound is more toxic to the kidneys than the organic compounds.

Gage (1964) studied the distribution and excretion of mercury after the subcutaneous injection of phenylmercuric acetate and of methylmercuric dicyanidamide in the rat. He found that phenylmercury is readily absorbed from the injection site and is rapidly removed from the blood by the tissues. Some concentration and probably some metabolism of phenylmercury occurs in the skeletal muscles, but the bulk is removed from plasma by the liver and the kidneys where it is rapidly metabolized and excreted with only a small proportion appearing unchanged in the feces and urine. Absorption of methylmercury was rapid from the injection site and was taken up by all tissues, especially in the skeletal muscle and intestine. The major route of excretion is through the gut, but the ratio of organic mercury in the liver and feces indicates methylmercury is also excreted by this route more slowly than phenylmercury acetate. With both methylmercury and phenylmercury, there is a high content of mercury in the hair; with methylmercury the concentration is greater than in any other tissue, and there may be an appreciable excretion of mercury by this route. There is no evidence whether the mercury is excreted in sebum or incorporated into the hair proteins.

The mouse excretes methylmercury in the bile and also *via* the intestinal mucosa (Berglund and Berlin, 1969). Clarkson (1970) demonstrated that the rat excretes methylmercury in the form of methylmercury cysteine in the bile. This is completely resorbed in the upper gastrointestinal tract, since none is detectable in the large intestine. The rate of turnover of epithelial cells may be a determining factor in the rate of excretion of methylmercury, since studies have shown some accumulation of mercury in the mucosal epithelium. The turnover of epithelial cells in rats is five times faster than the turnover in man. This correlates with the difference observed in rate of elimination of methylmercury in the two species (Berglund and Berlin, 1969).

Biotransformation of methylmercury to inorganic mercury occurs before excretion. About 40% of the total mercury excretion was found to be inorganic mercury. About 50% of the fecal excretion and from 5 to 20% of the urinary excretion is inorganic mercury. Enterohepatic circulation of mercury from methylmercuric chloride is important in the distribution and excretion of mercury. About 10% of an administered dose is excreted in the first day. This falls to about 3% by the 10th day. During this period only about 3% is excreted in the feces. Almost all of the mercury present in the bile was in the form of methylmercury cysteine and inorganic mercury bound to protein. The cysteine complex is rapidly and completely reabsorbed in contrast to the inorganic mercury. Other sources of mercury in the feces are the sheddings of intestinal epithelium, pancreatic secretion, and some secretion from the pylorous. Biotransformation within the intestinal lumen in the cecum is the major source of inorganic mercury in the feces.

Enzyme systems may participate in the metabolism of organomercurials. Studies by Clarkson (1969) indicate that different compounds release inorganic mercury at different rates. Paramercurbenzoate was metabolized the fastest and methylmercury the slowest of seven compounds studied. These studies indicate the nephrotoxic action of mercurials may be related to the rate of their biotransformation.

The metabolism of methylmercury has been studied in man by Aberg, *et al.* (1969). After the oral administration of $^{203}$Hg-labeled methylmercury, $^{203}$Hg was detected in the whole blood within 15 minutes and reached a maximum blood concentration within 6 hours. The blood/plasma quotient remained constant for 24 days. The orally administered methylmercury was almost completely absorbed. The principal route of excretion was by the feces with 13 to 14.2% of the dose excreted during the first 10 days and 33.4 to 34.7% of the dose excreted in 49 days. The urinary excretion was low and accounted for only 0.18 to 0.27% in 10 days and 3.29 to 3.33% in 49 days. Urinary excretion was still taking place at 71 days. The biological half-life of methylmercury in man was estimated at 70.4 to 74.2 days. During the 240-day test period, there was never any measurable amount of mercury in the sperm. Only traces of mercury were found in the hair. Step scanning revealed the main uptake of $^{203}$Hg was in the abdominal cavity with possible localization in the cerebellum. Whole-body measurements over a 240-day period did not reveal any marked difference in the biological half-life in any region. Miettinen, *et al.* (1969) fed burbot containing bound $^{203}$Hg methylmercury to humans. His results were similar to those reported by Aberg.

Mercury may be excreted by rats through volatilization. In an experiment designed to determine if mercury is lost from animals through volatilization, Clarkson (1965) injected $^{203}$Hg complexed with glutathione into the hearts of rats. The animals were placed in a chamber so constructed that urine, feces, and air circulating through the cage could be collected and analyzed for $^{203}$Hg content. As soon as the animals were placed in the chamber, volatile mercury began to build up in the air sampler. It was determined that the radioactivity in the air sampler was not due to volatile release from the urine and feces. In a series of experiments in which animals were given varying amounts of $^{203}$Hg, volatile excretion varied from 0 to 7% of the administered dose and averaged approximately 4%.

There seems to be a steady state between intake, distribution and excretion of mercury. Gage (1964) demonstrated that rats receiving repeated subcutaneous doses of phenylmercuric acetate reached a steady state by the end of the second week when excretion balanced intake. No significant amount of mercury was found in the brain. In contrast, rats receiving similar doses of methylmercury dicyanidiamide showed no indication of reaching a steady state after 6 weeks. Further, there was an accumulation of organic mercury in all tissues, particularly in the erythrocytes and the brain. Although these short-term studies with methylmercury failed to demonstrate a steady state, Berglund and Berlin (1969b) showed that the continuous administration of dietary methylmercury (1-5 ppm) to rats resulted in a steady state between body burden and excretion in about 6 months. At equilibrium, the daily excretion corresponded to about 2% of the body burden. There was a linear correlation between dose and body burden.

The highest concentration of methylmercury in the brain was 8 $\mu$ g/g of brain tissue. There were no effects on body weight or conditioned behavior and no pathologic or anatomic changes were observed.

### IV.D. **Chemical Interactions and Biological Activity**

Mercury is capable of combining with a wide variety of organic molecules. Because of its interactions with ligands present in proteins, it is a particularly potent enzyme inhibitor. The enzyme systems or other biologically important molecules known to be inactivated by mercury would include all of the essential chemical components of the cell.

The action of mercury depends upon biological factors, the chemical composition, and the structural as well as the functional organization of cells. In living systems, large numbers of reactive substances compete for traces of mercury. Each chemical constituent has a certain significance in relation to cellular function, but the relative importance of the individual substances in maintaining a specific function varies greatly. Consequently, mercury binding will occur simultaneously at "sensitive" and "insensitive" sites, and the toxic action may be produced by only a small proportion of the total mercury fixed. This tends to obscure the relation between mercury binding and pharmacological response (Passow, H., Rothstein, A., and Clarkson, T. W., 1961).

IV.D.1. *Cellular Level*— Cell structure governs the accessibility of sensitive ligands and decisively influences the time course of mercury action. The cell membrane as a diffusion barrier protects the cell interior from poisonous action of the metal. On the other hand, sensitive ligands located within the membrane structure or on the outer cell surface are separated from the large reservoir of protective complex-forming substances inside the cell. Therefore, functions associated with the cell membrane are particularly susceptible to the action of mercury.

The first reactions of mercury are with the ligands of the cell surface, with associated disturbances of membrane function. Next, a redistribution of the metal may take place. As mercury penetrates into the cell, additional effects develop; and the initially inhibited functions may begin to recover. The inactivation of one sensitive site usually induces a whole sequence of secondary changes which may ultimately affect the physiological state of the whole cell (Passow, *et al.*, 1961).

IV.D.2. *Organ Level* — All of the generalizations concerning the cells are valid when considering the actions of mercury on organ systems and on the intact animal. The matter is complicated by the fact that, in the organs, several cell populations of different susceptibilities may exist in a complex anatomical arrangement. In animals, the effective concentration of mercury at the cellular sites of damage and the time of exposure are determined by the patterns of absorption, distribution, deposition, and excretion (Passow, *et al.*, 1961).

IV.D.3. *Chemical Interactions* — Most heavy metals, including mercury, are capable of forming complexes with ligands containing sulfur, nitrogen, or oxygen as electron donors. Nitrogen is the preferred donor in the formation of coordination compounds. Oxygen rarely forms coordination complexes, but when present in such dissociable groups as carboxyl and phosphoryl, forms strong ionic bonds with heavy metals. In any living cell, the following ligands are present:

$—OH, —COOH, —PO_3H_2, —SH, —NH_2,$
—imidazole

These ligands, which form the integral parts of almost any molecule of biological significance, are frequently essential to the normal functioning of the cells. Mercury does not have the same affinity for the different ligands. While it apparently has little affinity for —COO-groups, it has high affinity for —$NH_2$ and —SH groups (Gurd and Wilcox, 1956; Klotz and Klotz, 1959).

Hydroxyl groups of water can participate in complex formation and in the formation of insoluble hydroxides. These complexes may have a very complicated structure, and their electrochemical behavior may be quite different from the behavior of simply hydrated ions. Chloride ions also form strong complexes with mercury (Sillen, 1949). Complications in pharmacological studies arises immediately after dissolving mercury in water. In addition, all the listed biological ligands contain dissociable protons. Mercury ions will replace these protons in complex formation (Passow, *et al.*, 1961).

Mercury binding by biological materials is strong but not specific with regards to the ligands. The only rules that can be established are concerned with affinities. Chelate formation may introduce specificity patterns that invalidate the lists of relative affinities (Martell and Calvin, 1952). Many metabolites like amino acids or dicarboxylic acids are capable of forming chelates. Chelate formation generally leads to an increase of association constants. Since chelating agents may exhibit high specificity toward mercury cations, the rules regarding orders of affinities of mercury for ligands can be applied to biological systems only with caution. For example, if mercury, which has a high affinity toward sulfhydryl groups, produces a pharmacological effect, it is not permissible to ascribe the effect to the inaction of sulfhydryl groups. The observations must be supplemented by studying the effects of additional sulfhydryl reagents (Calvin, 1954). The arrangement of ligands within a single macromolecule may also favor chelate formation. Chelates of high specificity play an important role in the inactivation of enzymes by metals (Malmstrom and Rosenberg, 1959).

IV.D.4. **Action on Enzyme Systems** — Mercury is potentially able to combine with all of the components of an enzyme system. The possibilities of metal interactions with the enzyme or with the enzyme-coenzyme-substrate complex are manifold, because of the presence of many reactive ligands. The reduction of enzyme activity is dependent upon the accessibility and on the functional significance of the various metal-binding groups. Of primary importance are the interactions with the ligands which are functional in bond formation with the components of the enzyme-substrate complex at the active center of the enzyme. Other changes are brought about by metal combination with groups linked to the active center. The metal bindings with no functional significance play an indirect role. By combining with mercury, they reduce the amount available for reaction with functional ligands, thereby affording protective action (Passow, *et al.*, 1961).

Summer and Myrback (1930) found that 90% inhibition of urease activity resulted when 50 atoms of mercury were attached to one molecule of urease. Only 15 atoms of silver were required to yield 95% inhibition. It was concluded that a large fraction of the mercury atoms bound to the enzyme is associated with ligands which play no role in catalysis. Thus in urease inhibition by SH-seeking metals chemical affinities, functional importance of ligands, diversion to "insensitive" sites, and accessibility of "sensitive" ligands all play a role (Passow, *et al.*, 1961).

Inhibitory effects of heavy metals may also result from interactions with ligands which are not directly involved in the active center of the enzyme. The binding of the mercury cation to the side-chain residues of the protein may result in electrostatic charge and a shift in the ionization constant of the active center, leading to changes in the catalytic activity (Klotz, 1959). The inhibitory effect of relatively high concentrations of $Hg^{++}$ on chymotrypsin have been attributed to changes in the polymeric forms of the enzyme (Green, Glander, Cunningham, 1952).

A second type of indirect action may be a consequence of structural changes in the protein. In the presence of mercury, oxygen uptake by hemoglobin increases, particularly at low $O_2$ pressures (Riggs, 1952). The author stated that the metal is not attached to the heme-ring but probably exerts its influence by changing the structure of the globin moiety of the hemoglobin molecule. More recently Resnik demonstrated that the addition of more than 10 equivalents of mercury per hemoglobin molecule produced marked changes in the absorption spectra and the rotary dispersion curves of both $HbO_2$ and metHb. The final product in both instances was similar to acid-denatured protein. He postulated that mercuric chloride is capable of reaction not only with the sulfhydryl groups but also the imidazole residues of hemoglobin (Resnik, 1964).

Cell membranes contain large quantities of lipids, mainly phospholipids. It is well known that very small amounts of heavy metals produce appreciable changes of surface tension and surface charge of lipid films. Alterations of these variables may be expected to lead to marked changes of permeability and metabolic activities of surface enzymes (Passow, 1961).

IV.D.5. *Action on Cells* — The cell membrane is the first and most important site of action of metals. Frequently, almost all of the metal applied is rapidly absorbed by the easily accessible ligands of the outer surface of the membrane. The interior of the cell, on the other hand, is protected by the membrane as a diffusion barrier and also by the many inert substances in the cytoplasm that can react with and divert the metal. Many of the metal-binding ligands are essential to the maintenance of the membrane as a diffusion barrier or are necessary for the functioning of the enzyme of the membrane. The general pharmacology of mercury, therefore, is largely concerned with pathological changes of functions associated with the cell membrane (Rothstein, 1959).

Studies with yeast cells have revealed much about the interaction of heavy metals with the ionized ligands on the cell's outer surface. There is strong evidence for the existence of three types of metal-binding ligands on the surface of the cell, namely sulfhydryl, phosphoryl, and carboxyl groups. Evidence indicates that ribonucleic acid is the source of the phosphoryl groups on the cell membrane. The sulfhydryl group is the principal binding site for mercury. Metal interactions with SH-groups lead to a generalized breakdown of the permeability of the barrier of the cell (Passow, *et al.*, 1961).

Several types of enzymes are located on the cell's outer surface. These include: enzymes that digest external substrates (such as invertase and phosphatases), enzymes concerned in active transport phenomena, and enzymes involved in membrane synthesis. These enzymes are probably found in all cells and have been verified in red blood cells. Because of their location, the enzymes of the cell surface are particularly susceptible to heavy metals.

Some sugars enter cells slowly by simple diffusion. Certain other sugars enter quite rapidly by a special mechanism. Evidence indicates that the entry mechanism involves a definite chemical specificity, that pairs of sugars compete with each other, that the kinetics of entry follow mass-law behavior, and that the entry is susceptible to traces of heavy metals.

Mercury often produces an all-or-none response in which no effect is observed until a certain threshold concentration is attained. The response once elicited is maximal for a given cell. The curves relating dose and effect do not represent the parameters of the chemical reaction of the metal and cellular receptors, but rather the distribution of thresholds in the population. A distribution equation, usually the normal curve, can fit the data, whereas a mass-law equation will not. If mercury is added to a suspension of yeast cells, rapid loss of potassium occurs. The defect in the membrane is not specific for potassium. It represents a general breakdown of the permeability barrier. The individual cells respond in an "all-or-none" fashion. The reason for this is that mercury is acting on sites maintaining structural integrity, possibly SH groups in the membrane. No single one of these ligands plays any measurable functional role. However, when many of these groups are cross-linked by reaction with mercury, the stress on the membrane is sufficient to destroy it as a permeability barrier. In other words, if groups of ligands acting in unison are essential for a particular function, all-or-none responses may occur (Passow, *et al.*, 1961).

Erythrocytes of man and rodents are readily permeable to glycerol. Entry of glycerol into the cells is prevented by traces of mercury. Mercury is probably temporarily fixed to ligands in the membrane that control glycerol permeability. Subsequently, it moves into the interior of the cell and combines with the many complexing substances. As long as some mercury is bound to the membrane, inhibition of glycerol takes place. The inhibition disappears as soon as all of the mercury has passed through the membrane. At very high mercury concentrations, the complexing ligands of the cell interior become saturated. The excess mercury remains attached to the cell membrane and a permanent reduction of glycerol permeability is produced (Passow, *et al.*, 1961).

Mercury inhibits the uptake of glucose by the rat diaphragm. The inhibition reaches a concentration-dependent maximal value in less than 20 minutes. After a lag of over 30 minutes, a second effect gradually develops: respiration becomes progressively inhibited, provided relatively high concentrations of mercury are applied. Upon addition of slowly penetrating complexing agents like BAL or cysteine, the inhibition of glucose transport can be reversed whereas that of respiration cannot. The respiration of muscle homogenates is reduced almost immediately on addition of mercury, and the inhibition can be rapidly reversed by the addition of cysteine. It appears that the metal first interacts with functional groups at the cell surface, therefore inhibiting the transport of sugar. Subsequently it slowly enters the cells, and the respiration is progressively inhibited (Demis and Rothstein, 1955). Studies of binding of mercury by rat diaphragm confirm this interpetation. Uptake of mercury by the excised diaphragm proceeds fairly rapidly for about 20 minutes. Thereafter, the rate of mercury uptake proceeds at a much lower rate constant. The time-sequence involves a rapid diffusion through the interstitial spaces and immediate binding on the cell surface, followed by a slow penetration through the membrane to the respiratory sites within the interior of the cell.

In epithelial tissues such as the small intestine and the kidney, several populations of cells are found in a definite geometrical arrangement. The actions of mercury here are more complicated than in a homogeneous population of cells. Similarities are found, however, because the absorptive and secretory functions of the epithelia represent specialized use of mechanisms present in nearly all cells. It can be stated that any observed inhibition of mercury of the net transport of salt solutions or of glucose across epithelia can be explained in terms of mechanisms similar to those active in the cells (Passow, *et al.*, 1961).

The action of mercury on the membrane of the columnar epithelial cells of the jejunum is similar to its action on the membranes of muscle and red blood cells. Immediately following the addition of mercury (as mercuric chloride) to the mucosal side, rapid responses are observed in the electrical potential across the intestine, the loss of cellular $K^+$, and the cessation of glucose uptake. Each of these responses is associated with the action of mercury on the membrane facing the lumen. After a delay period, other functions are inhibited. These include $Na^+$ and glucose transfer into the serosal solution and the production of lactic acid. Similar disturbances in electrolyte equilibrium have been reported for the action of mercury on kidney slices (Kleinzeller, *et al.*, 1957).

Mercury can produce one kind of response when added to the mucosal side of an epithelial tissue and a different response when introduced on the serosal side. When mercury at $10^{-4}$ M is in contact with the mucosal surface of frog skin, transport of salts and water is reduced, because of the specific inhibition of the sodium transfer system. Since the effects are noted at mercury levels which do not produce inhibition of cellular metabolism, it seems likely that the toxic action of mercury is mediated through a direct effect on the outward-facing membrane of the epithelial cells. When mercury is present on the serosal side in the same concentration, sodium transport is accelerated. This response has been attributed to an interaction of mercury with the inward-facing membrane of the epithelial cells (Passow, *et al.*, 1961).

IV.D.6. *Differences in Biological Behavior of Various Mercury Compounds* — Hughes (1957) offered a physio-chemical explanation for the differences in biological behavior of metallic mercury, inorganic mercury, and alkyl and arylmercury compounds. Hughes states that alkylmercury halide possesses both a stable carbon-mercury bond and the essentially ionic mercury-halide bond. Carbon-mercury bonds possess a wide range of stabilities. In general, aliphatic carbon combines more stably with mercury than aromatic carbon; however, both would appear to be sufficiently stable to resist usual physiological processes. The pharmacology of methylmercury halides may be discussed in terms of the affinity of methylmercury ion for biological substances. This affinity may be described by the equation:

$$CH_3Hg^+ + X^- = CH_3HgX$$

Relative affinities for various biological substances may then be obtained by comparing the equilibrium constants for this reaction.

$$K = \frac{CH^3HgX}{CH_3Hg^+ \quad X^-}$$

Hughes has measured some equilibrium constants and the values are given below:

**Association Constants of Methylmercury for Certain Ligands**

| Ligand | $RS^-$ | $OH^-$ | $I^-$ | $Br^-$ | $Cl^-$ |
|---|---|---|---|---|---|
| $Log_{10}$ K | 17 | 9.7 | 9.0 | 7.0 | 5.7 |

Equilibrium Constants of $CH_3HgI$ for several Proteins

| Protein | K x $10^{\circ}$ |
|---|---|
| Human serum albumin | 25 |
| Bovine serum albumin | 7 |
| Bovine oxyhemoglobin | 20 |
| Bovine carbonylhemoglobin | 6 |

Hughes argues that from the magnitude of these association constants, methylmercury ion can exist only in infinitesimal concentrations in biological solutions. Thus at pH 7, there must be 500 times as much methylmercury hydroxide as methylmercury ion. If chloride is also present at physiological concentrations (0.1M), Hughes calculates that there must be 100 times as much methylmercury chloride as methylmercury hydroxide. However, since all biological systems contain thiols, the extremely large association constant for this reaction must mean that all but traces of the mercurial will be bound to thiols, provided that they exceed the amount of mercury present. This is usually the case, since human blood plasma is 0.5 millimolar thiol, and the red cells contain 60 times as much sulfhydryl in their hemoglobin. Man's plasma alone should be able to combine with 1 1/2 M of mercurial containing 300 mg of mercury. Methyl mercury also has a strong affinity for many other groupings present in biological substances as discussed in the previous section (Hughes, 1957).

One can modify the relative affinity of the mercurials for various sulfhydryl compounds by replacing the $CH_3$ group with larger organic radicals and with organic radicals containing other functional groups. One may expect interference from a large grouping if the SH group were located in a "tight" part of the protein molecule, or if there were charges on groups adjoining the SH group; and if the mercurial carried an identical charge. If the mercurial carried the charge opposite to that of the region surrounding the SH group, the affinity should be increased. Similarly, after binding to SH, the mercuric ion still contains a free valence capable of combining with some other properly placed group. Therefore, in general, mercuric ions should bind more tightly than simple mercurials, and considerable variation in affinity should exist from protein to protein (Hughes, 1957).

Most of the thiols of human plasma can be accounted for by serum mercapto-albumin containing 1 thiol group per protein molecule. However, 5 to 10% of the total thiol content of human plasma is present in the form of small molecules. Thus a mechanism is provided for the egress of mercury from the blood stream in combination with one of the small diffusible thiols. Simple mercurials, such as methylmercury halides, are 100 times as soluble in lipids as water. The amount of mercury present at any one site must be small in the presence of thiol, a definite infinitesimal amount is always present, and if any leaves the system by dissolving in a lipoid membrane, more will dissociate from the protein-mercurial complex to maintain the equilibrium. It is thus possible for all the mercury to diffuse through the membrane: Hughes postulates that these mechanisms would explain the rapid distribution of methylmercuric halide to all tissues of the body. Other compounds of mercury show a different distribution pattern.

Larger compounds of mercury do not appear to be selectively soluble in lipid solvents: they seem to be of such large size as not to diffuse through pores in cell membranes. The upper limit of size for ready diffusion is not known: however, even glucose, an uncharged molecule, appears to enter cells only by active transport. In the case of charged molecules, even smaller molecules may be excluded.

The bivalency of inorganic mercury, despite its small size, may act to restrict further its diffusibility since, with both bonds clinging to protein, the amount of time when it is free for diffusion must be reduced still further. This bivalency may also explain its ability to coagulate proteins since, by bonding to adjacent protein molecules, it can link them together causing aggregation (Hughes, 1957).

# CHAPTER 5

# TOXICOLOGY OF MERCURY

## V.A. **Toxicity to Laboratory Animals**

The absorption, distribution, metabolism, excretion, and the action of mercury at cellular and subcellular levels has previously been discussed. This section will deal with the toxic effects of mercury on the intact animal.

V.A.1. *Acute and Subacute Toxicity* — The acute toxicity of inorganic mercury is greater than that of the organic mercurials, regardless of the route of administration. The arylmercury, alkylmercury, and the alkoxymercury compounds seem to be equally toxic. The symptoms of poisoning with alkylmercury compounds may appear several weeks after administration, but the toxicity is still less than that of inorganic mercury when the observation period is prolonged to 1 month (Swensson and Ulfvarson, 1963).

Swensson (1952) studied the relative acute toxicities of mercuric chloride, methylmercuric chloride, and methylmercuric dicyandiamide, intraperitoneally, in mice. In this study, mercuric chloride was found to be the most toxic. Thereafter, with decreasing toxicity, were phenylmercuric acetate, the alkylmercuric chlorides, and the alkylmercuric dicyandiamides. No difference in toxicity was noted between ethyl and methylmercuric chlorides. Methylmercuric chloride and methylmercuric dicandiamide were of equal toxicity by the intravenous route in rabbits. With repeated intraperitoneal injections of one-tenth to one-fourth of the Probable Lethal Dose (PLD), there was a gradual increase in the appearance of central nervous system effects. Histological studies revealed diffuse injuries in the CNS with all compounds tested (inorganic mercury was not included in this study). Gage and Swan (1961) demonstrated that only alkylmercury compounds gave evidence of neurotoxic effects which developed in survivors of the median lethal dose in animals receiving sublethal doses. Short term tests with methylmercury (10 to 90 days) showed that a daily intake of 0.4 to 1.0 mg Hg/kg of body weight caused neurological symptoms in rabbits, dogs, and cats (Lefroth, 1969). The acute toxicities of the mercurials are summarized in Table 1.

Methylmercuric chloride, suspended in olive oil, was administered to mice, orally via stomach tube, at levels of 4.6 to 100 mg Hg/kg of body weight. The animals at the lower levels (4.6 to 14.7 mg Hg/kg) received seven daily injections, while the animals at the higher dosage levels received only a single injection. Neurological symptoms appeared in two groups given one dose of 32 and 46 mg Hg/kg, respectively. In groups which received a dose larger than 46 mg Hg/kg, death occurred before any neurological symptoms could be detected. Mice receiving a dose less than 32 mg Hg/kg showed no neurological symptoms up to the 30th day after the dose was administered. Seven daily doses of 10 and 14.7 mg Hg/kg administered to two different groups of mice induced neurological symptoms; all mice from the latter group died within 5 days after the last dose was administered. Only one of ten mice died as the result of the lower dose. The dominant neurological symptoms related to cerebellar, or vestibulocerebellar regulation of movement of posture. A brain concentration of mercury of 20 μg/g of wet tissue was found only in those groups which had shown some neurological symptoms (Suzuki, 1969).

**Table 1. Toxicity of Various Compounds of Mercury***

| Compound | Animal | Route of Administration | Toxicity mg/kg |
|---|---|---|---|
| Inorganic | | | |
| Mercuric chloride | Rat | oral | 37 ($LD_{50}$) |
| " " | Mouse | sc | 23 " |
| " " | Mouse | iv | 7.6 " |
| " " | Rabbit | sc | 10 (LD) |
| Alkylmercury | | | |
| Ethylmercuric chloride | Mouse | ip | 16 ($LD_{50}$) |
| Ethylmercuric dicyandiamide | Mouse | oral | 19 " |
| Ethylmercuric phosphate | Rat | oral | 30 " |
| Ethylmercuric thioglycolate | Rat | ip | 20 " |
| Ethylmercuric thioglycolate | Rabbit | iv | 20 (MLD) |
| Ethylmercuric toluenesulfonate | Mouse | ip | 28 ($LD_{50}$) |
| Isopropylmercuric hydroxide | Mouse | ip | 12 " |
| Methylmercuric chloride | Rabbit | iv | 15 (LD) |
| Methylmercuric chloride | Mouse | ip | 20 ($LD_{50}$) |
| Methylmercuric dicyandiamide | Rat | oral | 32 " |
| Methylmercuric dicyandiamide | Mouse | ip | 20 " |
| Methylmercuric dimercaptopropanol | Mouse | ip | 22 (PLD) |
| Methylmercuric hydroxide | Mouse | ip | 17 ($LD_{50}$) |
| Methylmercuric propanediolmercaptide | Mouse | ip | 29 " |
| Arylmercury | | | |
| Phenylmercuric acetate | Mouse | ip | 13 ($LD_{50}$) |
| Phenylmercuric catecholate | Mouse | ip | 50-100 ($LD_{50}$) |
| Phenylmercuric dinaphthylmethane-disulfonate | Mouse | ip | 25 ($LD_{50}$) |
| Phenylmercuric dinaphthylmethane-disulfonate | Mouse | oral | 70 " |
| Phenylmercuric nitrate | Mouse | iv | 27 " |
| Alkoxyalkyl | | | |
| Methoxyethylmercuric acetate | Rat | oral | 16 ($LD_{50}$) |
| Methoxyethylmercuric silicate | Mouse | ip | 50 " |

*Adapted from Swensson and Ulfvarson (1963) and Spector (1955)

Suzuki (1969) administered methylmercuric acetate labeled with $^{203}$Hg dissolved in distilled water subcutaneously to mice daily for 10 successive days. The daily dose was either 50 or 100 $\mu$ g/$^{203}$Hg/mouse. During the course of the experiment, the mercury concentrations of the various organs and tissues did not reach saturation. The concentrations of mercury in the blood was constantly higher than that in the brain in the course of administration and for a short period after it, but the decrease of mercury concentration in the blood was faster than that in the brain. The biological half-life of mercury in the brain was calculated to be 7.2 and 6.2 days respectively and that in the blood 4.2 and 4.1 days respectively for the 50 and 100 $\mu$ g Hg/mouse.

Sebe, *et al.*, (1962) studied the toxicity of a series of alkylmercury compounds. Compounds of alkylmercury containing R-Hg or R-Hg-S with the methyl, ethyl, or n-propyl chain administered orally to rats were toxic to the central nervous system and induced paralysis of the legs. Iso-propyl compounds and other alkylmercury compounds with 4 or 5 carbon atoms were shown not to cause these injuries.

Meshkov, Glezer, and Panov (1963) studied the effects of lethal and toxic doses of diethylmercury on the kidneys of rats. In these experiments, albino rats were administered doses of 25 to 100 mg/kg of body weight of diethylmercury. The animals at the 100 mg/kg dosage level died within 24 hours and were found to have pronounced degenerative changes in the kidneys, involving primarily the proximal tubules. The loops of Henle and the straight tubules in the medulla were almost unchanged. The lower doses of 25 to 50 mg/kg produced similar renal changes in 10 to 20 days. The exact nature of the histochemical change produced depended upon the extent of the degenerative processes. In the early stages (sublethal doses), there is a decrease in the nuclear DNA concentration of the epithelial cells of the proximal and thin segments, while the cytoplasmic RNA content increases. Further changes in the tubules are accompanied by a marked reduction in the DNA and RNA content. Sublethal doses produced significant changes in the ultrastructure of the proximal tubular epithelium: appearance of large numbers of vacuoles in the cytoplasm, destruction of the membranes of the endoplasmic reticulum, swelling and splitting the cell membrane, and, most important, destruction of the mitochondrial apparatus, swelling of the mitochondria and granular disintegration of their cristae.

In the experiments cited earlier, Swensson (1952) limited his histological examinations to the central nervous system, particularly the spinal cord, although, the cerebellum was also examined. Cell injuries were demonstrated in the granular cell layer of the cerebellum, in the Purkinje's cells in the cerebellum and in the cells of the spinal cord. The same changes were observed with all compounds studied; methylmercuric chloride, ethylmercuric chloride, methylmercuric dicyandiamide, ethylmercuric dicyandiamide, and phenylmercuric acetate. No essential differences were noted between the compounds. Injury to the myelin sheaths in the spinal cord were noted as well as selective Marchi degeneration in the posterior columns of the cord. Swensson found that injury to nerve cells occurred even after very small doses. When the injuries were sufficiently extensive, nerve symptoms arose. The degree of severity was clearly connected with the degree of severity of the poisoning and, to some extent with the period of time elapsing after the administration of the compound.

V.A.2. *Chronic Toxicity* — Fitzhugh, *et al.*, (1950) showed, that although inorganic mercury compounds are more acutely toxic than organic mercury compounds, phenylmercuric acetate was more toxic, chronically, than was mercuric acetate. Significant toxicity in the form of kidney damage was observed from 0.5 ppm dietary mercury in the form of phenylmercuric acetate. Ten to twenty times this amount of mercury in the form of mercuric acetate was required to cause similar damage. Mercury was accumulated in the liver and kidneys of animals fed phenylmercuric acetate, although no damage of a functional nature was observed. There was considerably more mercury stored in these organs after feeding phenylmercuric acetate than after feeding mercuric acetate. The results indicated that as the mercury concentration increased 100 times, the organ concentration was increased only about 10 times for both compounds. This suggests that there is a saturation phenomenon present, with excretion increasing with the dose.

V.A.3. *Genetic and Teratogenic Effects* — Experimentally, in certain systems of plants and in drosophilia, organic mercurials may produce genetic mutations and chromosomal aberrations.

Organic mercurials cause c-mitosis in the cells of *Allium cepa* roots. The aryl and alkyl compounds are most active and produce this effect at levels as low as 15 x $10^{-7}$M. The alkoxyalkyl compounds are less active and produce a comparable effect at levels as high as $30 \times 10^{-7}$M. All of the mercurials studied produced c-mitosis, however, there was a difference in their effects. The aryl compounds gave rise to distinctly more bridges and fragments than the other mercurials. The phenyl compounds produced a higher frequency of multipolar spindles and other spindle irregularities than the alkyl of alkoxyalkyl compounds (Ramel, 1967). These compounds are 200 to 1,000 times more effective than colchicine in producing c-mitosis. Rats which have been maintained on methylmercury for up to 8 months and in which mercury has reached a steady state showed no chromosomal aberrations in the blood cells (Ahlberg, *et al.*, loc cit, Berglund and Berlin, 1969).

As a result of the c-mitotic action, polyploid as well as aneuploid cells occur. The mercurial compounds cause c-mitotic tumors, and hook-like growths of the roots are also observed, which represent incomplete tumorous action. Fahmy reported studies on the cytologic effects of organic mercury compounds, the results of which are in agreement with the results given by Ramel. In addition, inorganic mercury is about 200 times less effective than organic mercury in the production of c-mitosis (Nelson, *et al.*, 1971).

In a study with *Drosophila melanogaster*, selected so that dysfunction of the sex chromosomes in either the female or the male would result in non-yellow (XXY) daughters or yellow (Xo) sons, treatment of the female larvae with aryl or alkylmercury resulted in a significant increase in the number of exceptional daughters (XXY) showing irregularities of meiotic chromosomal disjunction (Ramel, 1967). It has been shown that methylmercuric hydroxide binds to DNA and causes irreversible denaturation of DNA *in vitro*. Therefore, it may be suspected that methylmercury could induce mutations. Following the results of the Drosophila study, Ramel (1969) concluded methylmercury induces mutations, but the mutagenic effect should be considered minimal. He considers the genetic risks may be recognized at two levels. First, if a sufficiently high concentration should reach the gonads, a segregation disturbance like the one with Drosophila may occur. In these cases, one may expect the human defects will increase which are caused by the additional chromosome, e.g., Down's Syndrome or Klinefelters Syndrome. Secondly are the teretogenic effects of methylmercury; the accumulation in the fetus may cause disturbances in chromosome segregation during development (Ramel, 1969).

As reported earlier, rats which have been maintained on methylmercury for 7 to 8 months, until a steady state for mercury is reached, showed no chromosomal aberrations in any blood cells.

Oharazawa (1968) carried out investigations on the effects of ethylmercuric phosphate on mouse embryos with particular emphasis on embryopathy, teratology, and cytogenetics. Prior to the experiments, the $LD_{50}$ of ethylmercuric phosphate was determined as 76 mg/kg for the normal, nonpregnant female mouse of the ICR-JCL strain. To study possible fetal malformations induced by ethylmercuric phosphate, 40 mg/kg of the compound was injected subcutaneously on the 10th day of pregnancy. Controls received only distilled water and no other treatment. On the 19th day, the mice were sacrificed and the fetuses removed for comparison between the two groups. There were no differences between food and water intake of the two groups. The incidence of young from one litter was not significant. The weights of the young in the treated group were decreased. There was a 31.6% incidence of cleft palate among the treated mice, but no malformations of the bones or skin were found. The mice were similarly treated with ethylmercuric phosphate for the chromosome studies. Sacrifice was at 5,9, and 19 days. Using the plasma clot method, the number of cells from the two groups was compared with normal for abnormal chromosomal patterns. The incidence of unstable chromosomes characterized as polyploid, chromatid gap, or fragmented was 19.3% on day 5; on day 9, this incidence was 16.6% compared to 3.2% for the control group.

Murakami, *et al.*, (1955) investigated the teratogenic properties of phenylmercuric acetate, an ingredient of a vaginal contraceptive product, in mice. One-fourth of a vaginal contraceptive tablet containing phenylmercuric acetate was placed in the vaginas of mice on the 7th day of pregnancy. In another group of mice, an aqueous solution of the tablet with the corresponding amount of phenylmercuric acetate was injected subcutaneously on the 8th day of pregnancy. A control group of mice was also utilized. The rate of occurrence of abnormalities was highest in the mice which received phenylmercury vaginally (15.1%) and lowest in the controls (2.7%). The group receiving phenylmercury subcutaneously was intermediate between the two (9.1%). Clegg (1970) reported that the administration of a single dose of 14 mg/kg of body weight of methylmercuric phosphate to pregnant rats on the 10th day of pregnancy resulted in reduced body weight of the offspring and an incidence of 31.6% cleft palates.

### V.B. **Toxicity to Humans**

The symptoms resulting from poisoning with the inorganic mercurials differ in essential points from those resulting from poisoning with the organic mercury compounds. The symptomology of human poisoning with both types of compounds resembles that seen in laboratory animals.

V.B.1. *Inorganic Mercury Compounds* — Soluble inorganic compounds of mercury are irritating to the skin and mucous membranes. This effect is marked with mercuric chloride. Concentrations of 1 to 5% cause irritation, vesiculation, and corrosion of the skin and mucous membranes. More dilute solutions produce irritation to sensitive skin. Mercuric chloride may be absorbed from the intact skin and mucous membranes to the extent of producing symptoms of poisoning (Bidstrup, 1964).

V.B.1.1. *Acute Poisoning* — The oral ingestion of doses as low as 0.5 g of mercuric chloride has produced death. The mean lethal dose in adults is probably between 1 and 4 g (Gleason, Gosselin, and Hodge, 1963.)

When ionizable mercuric salts are ingested, necrosis begins immediately in the mouth, throat, esophagus, and stomach. Within a few minutes, violent pain, profuse vomiting, and severe purging is experienced. The patient may die within a few hours from peripheral vascular collapse secondary to fluid and electrolyte losses. If the patient survives this phase, the primary gastroenteritis subsides spontaneously within a few days. A second phase, developing within 1 to 3 days after exposure, is characterized by stomatitis, membranous colitis, and tubular nephritis. This second phase which is seen even in noncorrosive preparations of mercury is independent of the portal of entry, and is associated with a slow and prolonged excretion of mercury by the salivary glands, the gastrointestinal mucosa, and the kidneys. Death in this phase is usually the result of complete renal failure (Gleason, Gosselin, and Hodge, 1963). Postmortem examination shows inflammation and corrosion along the alimentary canal and severe damage to the kidneys. The glomeruli as well as the tubules are involved (Goldwater, 1957).

V.B.1.2.*Chronic Poisoning* — The most frequent manifestations of chronic inorganic mercurial poisoning are (1) gingivitis and stomatitis, often associated with loss of teeth; (2) tremor, involving the hands and later other parts of the body; and (3) personality change known as erethism. This condition is characterized by irritability, bursts of temper, and excitability, sometimes alternating with depression. There are numerous other signs and symptoms including salivation, loss of appetite, weight loss, weakness, and disturbances of urinary and gastrointestional function (Goldwater, 1957).

There is little or no correlation between urinary mercury levels and severity of symptoms. While urinary mercury levels may give some indication of the degree of exposure, they are of limited value in diagnosis of poisoning, since high levels can be found in human subjects who are symptom free, and low levels in those exhibiting marked evidence of mercurialism. Albuminuria severe enough to result in nephrotic syndrome can occur (Goldwater, 1957).

V.B.2. *Organic Mercury Compounds* — The organic compounds of importance in pesticides are the aryl and alkylmercury compounds.

V.B.2.1. *Arylmercury Compounds* — Cases of clinical poisoning with phenylmercury salts are rare in the literature in comparison with inorganic and alkylmercury compounds. However, the toxicity of the phenylmercuries can not be discounted. One may conclude from the animal data that these compounds are highly toxic. In addition, since phenylmercury is metabolized to inorganic mercury in the liver, one may expect kidney involvement resulting from toxic doses of the compound. Phenylmercuric acetate is irritating to the skin and may also produce a delayed sensitivity (*Sunderman, et al.*, 1956). Hypersensitivity has been reported to occur with several phenylmercury salts (Matthews, 1968). Acrodynia (Hirschman, *et al.*, 1963; Matthes, *et al.*, 1958; Schrager, 1964) and neuromyasthenia (Miller, *et al.*, 1967) have been reported from inhalation of phenylmercury vapors from paints. Dunn reported four cases of mercury poisoning resulting from the use of fiber glass air filters containing phenylmercury acetate from forced draft heaters. Becker, *et al.*, (1962), reported on 5 cases of nephrotic syndrome associated with contact with mercury. Three of these cases involved the use of ammoniated mercury ointment, one associated with the use of phenylmercury paint additive, and one with a mercurial diuretic.

V.B.2.2. *Alkylmercury Compounds* — If alkylmercury compounds come in contact with the skin, dermatitis may develop. The first symptoms are warmth, swelling and a burning sensation. Later, blisters may form which may break, producing a sodden, grayish-white appearance. These symptoms may occur at any time, from a few days to several weeks, after the first contact. Irritation of the mucous membranes of the nose, mouth and throat are often described in connection with alkylmercury compounds. These sensations may come after a short exposure and usually disappear quickly when the exposure is terminated (Lundgren and Swensson, 1949).

V.B.2.2.1. *Acute Poisoning* — In acute alkylmercury poisoning, symptoms of involvement of the respiratory tract and the alimentary tract are described. Headache, fatigue, and other nervous symptoms have been reported. Myalgia has been noted and albuminuria is a transient symptom (Lundgren and Swensson, 1949).

V.B.2.2.2. *Chronic Poisoning* — In chronic poisoning, symptons are fatigue, headache, impairment of memory and of concentration, numbness and tingling of lips and tongue and later of the limbs, slurred speech, increasing ataxia and impaired gait. There may be concentric narrowing of the visual fields and impairment of hearing. The symptoms may first appear as long as 2 months after the exposure has ceased. The sympsoms may increase, remain static, or decrease. In cases of severe poisoning, the physical defects and the mental deterioration often remain. This clinical picture has been reproduced in animal experiments (Lundgren and Swensson, 1949).

The clinical details of the Minamata, Japan, and the Alamogordo, N. Mex., poisonings have been reported by Takeuchi (1970) and Gregg, *et al.*, (1971), respectively.

# CHAPTER 6

# ECOLOGIC EFFECTS OF MERCURY CONTAMINATION

Sources of mercury in the environment, both natural and man-made have been considered. While all forms of mercury are toxic to life, it has been pointed out that arylmercury, or methylmercury specifically, has the most profound effect on animal life. It has been demonstrated that all forms of mercury may be transformed into methylmercury in an aquatic environment.

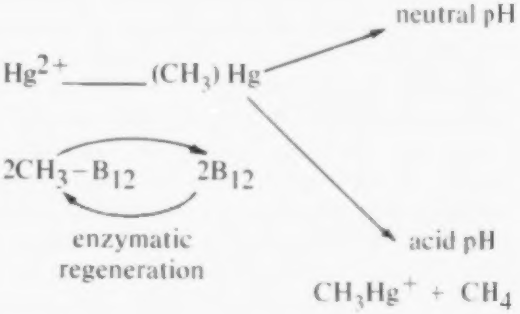
VI.A. **Biotransformation of Mercury** — The methylation of mercury in sediments in river and lake bottoms is the process which, to a substantial degree, is responsible for current and potentially future contamination of aqueous systems and their associated biota. Indirectly this methylation process may also play, through the evaporation of dimethylmercury, a large role in atmospheric transport of mercury.

Natural methylation of mercury was suspected in the Minamata episode (Fujiki 1963 cited in Wood, *et al.*, 1968), but the suspicion was put aside as being of no significance when methylmercury was identified in the discharge from the acetaldehyde plant (Irukayama, *et al.*, 1962). Mercury has been shown to be methylated by aquarium and natural sediments (Jensen and Jernelov, 1969) and enzymatically by extracts of methanogenic bacteria (Wood *et al.*, 1968). These workers also found that small amounts of methylmercury were produced nonenzymatically. Both groups found both monomethyl and dimethyl mercury as initial products, with high mercurial concentration favoring the monomethyl form (Wood *et al.*, 1968), and alkaline pH favoring the dimethyl form (Larsson 1970). The latter compound decomposes to monomethyl form at an acid pH. Jensen and Jernelov (1968) suggest that the methylation might proceed as follows:

$$Hg^{2+} \longrightarrow CH_3Hg^+ \longrightarrow (CH_3)_2Hg$$

$$Hg^{2+} \longrightarrow (CH_3)_2Hg \longrightarrow CH_3Hg$$

Wood *et al.*, (1968) suggest the following scheme of methylation by *Methanobacterium omelianskii* or by solutions of methylcobalamin:



The tendency of alkaline pH to favor a higher production of the more volatile dimethyl form also would produce a larger discharge of methylated mercury by evaporation into the atmosphere; contrarily, a more acid pH should then favor (1) a higher proportion of the less volatile monomethyl form, (2) ready decomposition of the smaller proportion of the dimethyl compound, and (3) a greater total retention, with less loss to the atmosphere (Larsson 1970). These mechanisms have been cited as possible factors (Hohnels 1970) leading to the contamination of remote acid lakes with high levels of mercury in fish, in the absence of known sources of contamination. All forms of mercury appear to be directly or indirectly capable of conversion to methylmercury (Jernelov 1969).

Jernelov suggests that phenylmercuric acetate slimicides are more efficient sources of mercury for subsequent methylation than is inorganic mercury.

Although methylation of mercury will occur anaerobically, it appears to be more efficient in aerobic systems.

VII.B. **Sweden** — Wildlife served its traditional role as an early warning system for man when problems with mercury arose in Sweden. About 1955, several ornithologists in various parts of Sweden observed a decline in the populations of some seed-eating birds. The increase in the number of birds of prey found ill or dead also attracted attention. In 1958, Borg drew attention to the fact that birds found dead and sent to the State Veterinary Medical Institute had remarkably high residues of mercury in their livers and kidneys. Studies of shot and trapped birds also revealed high levels. The conclusion was that the large numbers of dead specimens of seed-eating birds (pheasants, partridges, pigeons, finches) and birds of prey (eagles, buzzards, hawks, falcons, owls) in particular, and of corvine birds indicated a very general poisoning in birds. The source of the mercury was attributed to the use of mercury compounds in agriculture. The decline in the population of several bird species in Sweden was attributed to the use of pesticides (Johnels and Westermark, 1969). News of the Minamata problem in Japan led to broader and deeper studies (Nelson, *et al.*, 1971).

Analyses soon revealed that mercury pollution was serious in Swedish lakes and rivers and that seed dressings were not the sources of this contamination. Waste and leakage from pulp mills and chlor-alkali factories were chiefly responsible. The result was local and spotty contamination, often heavy. Many lakes and streams remained free or nearly free of mercury. Even today, most waters of Sweden are not and need not be monitored. This localization of contamination means that one must look at the right spots to find it. Early efforts to repeat the Swedish findings in the United States, failed because the animal samples that were taken did not come from near sources of mercury, despite the fact that they were taken from some of the most polluted estuaries of the eastern United States (Nelson, *et al.*, 1971).

It was evident in Sweden that mercury from seed dressings was responsible for the decline of seed-eating birds. The birds of prey obtained their high levels of mercury from fish. As stated above, the levels of mercury in the rivers and streams arose chiefly from industrial waste and to a smaller extent from agricultural runoff. Mercury levels up to 9.8 ppm were recorded in Swedish fish.

It became apparent that mercury contamination of the Swedish environment was even more widespread than had been previously believed. In order to assess the historical development of this contamination, neutron activation analyses of the mercury content of bird feathers from museum specimens collected over the previous century were performed (Johnels and Westermark, 1969). These studies revealed that in birds with a terrestrial food chain, a nearly constant level of mercury was maintained from the middle of the previous century until 1940. Subsequently, an increase in the mercury concentration of feathers occurred amounting to at least 10 to 20 times the previous level. Shortly after 1940, liquid treatments for seed grain using alkylmercury ingredients replaced dusting with other types of organic mercury compounds in many of the developing nations, because of the reduced hazards and inconvenience to operators dressing grain with specially designed machines. The simultaneous appearance of increased mercury accumulations in birds with a terrestrial food chain thus suggests that the alkylmercury seed-dressings are the main source of contamination of the terrestrial environment. In contrast, fish-eating birds showed a gradual increase in mercury content since the previous century, suggesting that the mercury contamination of water follows the general increased industrial activity (Wallace, *et al.*, 1971).

In 1966, Westermark, *et al.*, demonstrated that part of the mercury content in bird's feathers is metallo-organic. In 1967, Noren and Westöö demonstrated that almost all mercury present in fish muscle appears in the form of methylmercury (Johnels and Westermark, 1969). Methoxyethylmercury compounds were substituted for alkylmercury compounds in seed-dressing formulations after February 1966, and the relative amount of dressed seed used for sowing was also reduced from 80% (prior to 1966) to 12% (1967). These changes apparently had no deleterious effect on crop yield. In 1966 and 1967, the mercury levels in the feathers of predatory birds with a terrestrial food chain abruptly dropped to levels about 50% above those typical for the previous century (Wallace, *et al.*, 1971).

VI.C. **Canada and the United States** — In 1967, a limited study of mercury residues in U.S. foods was conducted by the Food and Drug Administration as part of the Pesticide Total Diet Study. Six food classes were analyzed by neutron activation analysis, and the results indicated background level of mercury in the order of 0.002 to 0.050 ppm. No further testing was performed in this country until 1970. In 1969, following warnings of significant mercury pollution in the central provinces, studies were initiated by the Canadian Wildlife Services to define the situation. Shortly thereafter, several commercial catches of fish (walleye, northern pike, bass, and jackfish) taken from Lake Winnipeg, Cedar Lake, Saskatchewan River, and Red River in the Province of Manitoba were detained by the Canadian Federal Department of Fisheries and Forestries, because they contained mercury residues ranging from 5 to 10 ppm. As a result of concurrent testing by Ontario officials, the Canadian Government publicly embargoed all commercial fish taken from Lake Saint Clair effective March 23, 1970.

On April 10, 1970, a formal monitoring program was initiated by the United States Food and Drug Administration in all 17 of its districts. All of the 75 known, chlor-alkali plants in the United States were visited. Agricultural run-off and other industrial sources of pollution were also examined during the investigation. When the industrial process was suspected of polluting water, samples of fish were collected and analyzed to determine the impact of the contamination on the environment. Any fish exceeding the interim guideline level of 0.5 ppm mercury in commercial channels were recommended for seizure (Mercurial Pesticide Review Panel Report, 1971).

The majority of the fish analyzed have been collected from areas where investigations have shown contamination with mercury wastes. Of 763 composite samples of fish examined by the Food and Drug Administration, 683 samples were below 0.5 ppm mercury, while 124 were above. The highest mercury residue thus far encountered was a Lake Onondaga catfish composite which was found to contain 4.3 ppm. In areas such as the Rocky Mountains with no known pollution sources, "background" can run as high as 0.2 ppm mercury but averages less than 0.1 ppm, depending upon the species (Mercurial Pesticide Review Panel Report, 1971).

The Review Panel reached the following tentative conclusions on mercury contamination of the environment:

(1.) Where there are chlor-alkali plants, there is a great possibility of mercury escaping into the environment. Since fish have a great propensity for bioconcentration of mercury, the fish level reflects the degree of pollution of the water.

(2.) The mercury content of fish is related to the species, the size, locality, and length of exposure to mercury.

(3.) Agricultural runoff from areas where heavy use has been made of mercury-treated seeds can result in residues in fish greater than 0.5 ppm mercury.

A systematic survey of wildlife and animal food products (including freshwater and marine fish) has been underway in Canada, and the initial results were made available in the summer of 1970. At that time, using neutron activation analysis, elevated levels of mercury were found in several pheasants from Alberta and in pike, pickerel, and whitefish from the Great Lakes area. Avian products generally contained less than 0.05 ppm, and most fish (except those from heavily contaminated areas) averaged 0.2 ppm or less. The levels of mercury found in these fish were omewhat lower than those found by other laboratories, and the explanation given was that smaller fish were sampled for analysis.

In the fall of 1970, the United States Food and Drug Administration found that canned tuna sold in the United States contained up to 1.2 ppm mercury (average 0.37 ppm) and that frozen swordfish ranged from 0.18 to 2.4 ppm (average 0.93). Surprisingly high levels (25 - 170 ppm) were also found in livers of fur seals and sea lions off the western coast of North America. A 21 member *ad hoc* committee of experts reviewed the FDA's data on mercury contamination in swordfish and suggested that swordfish consumption be curtailed in the United States. In May 1971, the Food and Drug Administration issued the statement that the "public stop eating this fish until and unless the situation can be remedied."

VI.D. **Mercury in Fish** — In Sweden, the pike contain two to three times more mercury than do the other fish in the same waters. This fish is taken as the standard for blacklisting waters. A body of water is blacklisted in Sweden when a sample of five pike shows residues of 1 ppm or more of mercury in most of the five. If one or two of the five have a higher level, another sample may be requested. Statisticians have advised a sample of at least 11, but costs would be prohibitive. At present, the judgment is made more or less subjectively from the sample of five. If residues are between 0.2 and 1 ppm, Swedes are advised to eat fish from these waters no more often than once a week. The Swedish action level of 1 ppm is considered too high, but if 0.5 ppm were the criterion, as in the United States and Canada, five times as many waters would be blacklisted and monitoring costs would be extravagant (Nelson, *et al.*, 1971).

When comparing residues of mercury for blacklisting purposes, levels in pike are adjusted to fit a pike weighing 1 kg., or about 2.2 pounds. This is done, because pike keep growing and keep increasing in concentration of mercury. The curve of the increase in the level of mercury tends to flatten in large, old pike, but it does not seem to reach a steady state (Nelson, *et al.*, 1971).

Fish and shellfish found dead at Minamata contained 9 to 24 ppm mercury on a wet-weight basis. One Swedish pike was taken which contained 17 ppm, however, pike have been killed experimentally at muscle levels of mercury of 5 to 9.1 ppm. Stickel (Nelson, et al., 1971) states that there is clearly an overlap between the curves of residue distribution in living wild pike and experimentally killed pike. He believes that Swedish pike have died from mercury poisoning in the wild, and losses were gradual and unobserved.

The lethal concentration of mercury compounds found for various aquatic organisms is listed in the appendix. While such information indicates that mercury compounds are remarkably toxic at low concentrations, it does not define the maximal levels which should be avoided to maintain a healthy aquatic ecosystem. While 60 ppb ethylmercury is lethal to marine phytoplankton, as little as 0.1 to 0.6 ppb alklymercury introduced into seawater will produce a measurable inhibition of photosynthesis and growth. It appears that concentrations of mercurial compounds well below the proposed water-quality standards of 5 ppb can have a detrimental effect on phytoplankton (Harriss and White, 1970). The authors also conclude that the use of organomercurial compounds in any way that permits their discharge into natural waters should be stopped as soon as possible. The long-term effects of mercury pollution below concentrations of 1 ppb must be determined to establish adequate water-quality standards. In another study, half of the goldfish continuously exposed to a concentration of 820 ppb mercuric chloride died within 7 days, yet an exposure for only 2 days to 3 ppb mercuric chloride produced a measurable impairment in learning behavior (Weir and Hine, 1970).

VI.E. **Mercury in Birds** — Stickel, in "Hazards of Mercury" (Nelson, *et al.*, 1971), gives an excellent account of the effect of mercury on birds in Sweden.

According to Stickel, birds have been seriously affected by mercury in Sweden. Treated seed had the most dramatic effect, while aquatic contamination had less sudden and dramatic effects. The world-wide ramifications are just beginning to be known.

The acute toxicity of methylmercury to birds results from levels about the same as those toxic for laboratory mammals, around 12 to 20 mg/kg of body weight. Chronic tests with birds have been carried out largely with seed operationally dressed with about 15 to 20 ppm methylmercury. These seed killed pheasants in 29 to 61 days and jackdaws in 26 to 38 days.

Mercury residues in liver-kidney composites of birds killed experimentally with treated seed ranged from 30 to 130 ppm for pheasants, 70 to 115 ppm for jackdaws, and 50 to 200 ppm for magpies. Muscle levels in pheasants ranged from 20 to 45 ppm. Stickel concludes that kidney-liver residues of 30 ppm or more in birds indicated critical exposure and perhaps death; normal levels, by contrast, are less than 1 ppm. Using these criteria in judging wild birds, both those found dead and those taken alive, more than half the bird populations of Sweden were carrying increased levels of mercury and many birds had died outright. Population declines occurred in a number of species (Nelson, *et al.*, 1971).

Stickel reported that Tehning demonstrated that pheasants could readily eat enough dressed seed to create the observed tissue levels of mercury and to cause death. Seed is often available on the surface, especially at the turn-around areas at the ends of fields. The effects of mercury were complicated by the presence of aldrin and dieldrin in the seed dressing, and the amount of aldrin and dieldrin in the birds was not determined. The use of aldrin or dieldrin is no longer legal in Sweden.

Stickel also reports that while seed-eating birds were declining, predatory birds that fed on them—or on fish—were in a worse situation. He states that all studies he has seen support the view that free and protein-bound methylmercury acts in the same way and with equal force (Nelson, *et al.*, 1971).

Hawks and owls were hard-hit. Wild seed-eaters had liver residues ranging up to 140 ppm, but predatory birds had levels up to 300 ppm. As predatory birds are rarely numerous and have relatively low reproductive rates, they might have been exterminated over large areas, if the release of mercury had not been stopped. However, since the ban on seed dressing with methylmercury took force in 1966, goshawks have been recovering, and their residues of mercury have dropped (Nelson, *et al.*, 1971).

Stickel reports that the seed-eaters responded more promptly, and that levels of mercury in pheasants were back to normal the year after the ban. The methoxymethylmercury dressings which are now used (only when and where needed) are less toxic and are much more easily excreted than are the methylmercury dressings.

The half-life of mercury in birds does not appear to be excessive by comparison with that in mammals. The half-life in chickens is 35 days. Male quail excrete mercury slowly, while the female excretes it much more rapidly due to excretion in eggs. Pheasants have a relatively rapid loss of mercury.

The reproduction of birds has been greatly reduced by dietary exposure to mercury. Hatchability is reduced, but there appears to be no drop in egg production. The pheasant eggs with demonstrated poor hatchability contained 1.3 to 2 ppm mercury.

VI.F. **Mercury in Farm Animals** — There are a few reported injuries of livestock from the feeding of mercury-treated seed grain. Loosemore, *et al.*, (1967), reported experimental results with pigs fed grain treated with 6 ppm mercury. Pigs which survived 10 to 21 days on the mercury-treated grain suffered tubular necrosis of the kidneys, and their livers contained 60 ppm mercury. Their kidneys contained 65 ppm mercury.

Trabash (1970) reported condemnation of 7 cattle carcasses in Oregon, because of mercury content. The kidneys of one of the animals contained 67 ppm mercury; muscle ranged from 0.1 to 1.63 ppm among the 7 carcasses. Kahrs reported on a herd of swine fed for several weeks a diet one-half of which consisted of seed grain treated with methylmercuric dicyandiamide. Almost all of this herd of 44 adults and 5 litters of pigs died within a 3 month feeding period (Mercurial Pesticide Review Panel Report).

Westöö (1967) reported that hens fed grain treated with methylmercury lay eggs with higher mercury content than those fed grain treated with alkoxyalkyl mercury compounds. Tehning (1967) found that hens fed grain containing 18.4 ppm methylmercury in half their feed intake laid eggs with more than 20 ppm methylmercury in the albumin. Other workers have reported lower amounts of methylmercury in eggs of chickens fed treated grain.

# CHAPTER 7

## THE HAZARDS OF MERCURIAL PESTICIDE USE

Approximately one million pounds of metallic mercury were used in the United States in 1969 in the production of pesticide chemicals. About 85% of this one million pounds was used in preserving and mildew-proofing paints while the remainder was used in agriculture, the paper and pulp industry, and in miscellaneous pesticides. The pesticide uses of mercury are the largest dissipative or nonrecyclable uses in this country today.

Elemental, inorganic, and organic mercury are used in pesticides. The organic compounds that have gained importance all have the general structure R-Hg-X, where R is an organic radical, alkyl, alkoxyalkyl, or aryl. The group X is bound to mercury with a bond more or less having the character of a salt and originating from organic or inorganic substances with dissociable hydrogen ions, e.g., acids, amides, phenols, or thiols. At present, some hundred combinations of different organic radicals and anions are used in commercial preparations of mercury fungicides.

The different compounds of mercury differ in their solubility, volatility, and their toxicity to man and animals. Therefore, in consideration of the hazard of a particular use, both the nature of the compound and the usage pattern must be considered.

### VII.A. **Cancelled or Suspended Uses**

Steps have already been taken that have reduced or eliminated certain uses of mercury.

VII.A.1. *Paper and Pulp* —The paper and pulp use fell sharply in 1965 consequent to Food and Drug Administration action requiring that paper used to wrap food be free of mercury. Although, the 1969 paper and pulp use was above the 1968 level, it was only 25% of the 1964 level. This use will be reduced to zero as the result of the August 7, 1970, cancellation of the registered uses of all mercury products bearing the claims or directions for use as slimicides, algicides, or for use in laundering. These cancellations were based on the potential of these uses to result in contamination of water.

VII.A.2. *Alkylmercury Seed Treatments*—As a result of the poisonings in Alamogordo, N. Mex., which resulted from the ingestion of pork from hogs fed seed treated with cyano (methylmercuri) guanidine, all registrations of products containing this compound were suspended February 18, 1970. On March 4, 1970, and *ad hoc* committee appointed by the National Academy of Sciences, National Research Council recommended that all compounds containing a short chain alkyl group bonded chemically to a mercury atom through a carbon-mercury bond should be considered toxicologically alike regardless of the associated anion until proven otherwise by a detailed review of appropriate data. Accordingly, a notice of suspension of the registrations containing alkylmercury compounds bearing directions for use as seed treatments was issued March 9, 1970.

VII.A.3. *"Zero Tolerance" and "No Residue" Registrations* —The registrations of products containing hydroxymercurichlorophenol bearing directions for use on vegetable and field crop seeds, the registrations of products containing hydroxymercurinitrophenol bearing directions for use on potatoes and sweet potatoes, and the registrations of products containing phenylmercuric acetate or phenylmercuric ammonium acetate bearing directions for use on applies, cherries, peaches, strawberries, and sugarcane were cancelled by the March 12, 1971, PR Notice. These cancellations were the result of implementing the recommendations of a National Academy of Sciences, National Research Council Advisory Committee to abolish "no residue" and "zero tolerance" registrations. Registrations are being continued on certain other pesticides based on pending petitions for finite tolerances or upon request of a Federal Agency.

VII.A.4. *Algicide Use in Swimming Pool* — Aglimycin 200 and Algimycin 300 are products containing phenylmercuric acetate for the control of algae in swimming pools. These products were first registered in 1962, under protest, as provided in the Federal Insecticide, Fungicide, and Rodenticide Act of 1947. It was the decision of the United States Department of Agriculture that the registrant had not clearly demonstrated the safety of the products. Termination of the registrations was affected in 1964, pursuant to Public Law 88-305 eliminating registrations under protest. The firm reapplied for registration in 1964 with supplemental data. Questions were raised by the United States Department of Agriculture, Food and Drug Administration, and the Public Health Service regarding the data submitted by the firm purporting to show an adequate margin of safety to humans when used as directed. The products were registered in 1965 with the provision that specific additional data would be submitted. Since that date, registrant has failed to furnish all the data set forth by the United States Department of Agriculture. Notice of cancellation of the registrations for Algimycin 200 and Algimycin 300 was made on July 22, 1969. The registrant requested an advisory committee to review the cancellation action.

### VII.B. Currently Registered Uses

In May 1970, the Department of Health, Education, and Welfare, acting under the provisions of the Interagency Agreement on Pesticide Registrations, requested the formation of a registration review panel for the purpose of considering the current registrations of mercurial pesticides. As provided by the Interagency Agreement, the panel was composed of representatives of the Department of Agriculture, the Department of Interior, and the Department of Health, Education, and Welfare.

The panel was dissolved on January 20, 1971, following the transfer of all pesticide responsibilities to the Environmental Protection Agency. However, the panel submitted their report, although incomplete, so that it would be available to those responsible for pesticide regulatory activities.

This report, "A Report on the Mercury Hazards in the Environment," contain no unified recommendations for actions to be taken with the currently registered uses of pesticides. However, it does contain recommendations from the individual panel members. Without exception, the members recommended cancellation of the registrations of all alkylmercury containing pesticides. The members were also in agreement that only the registrations for essential uses of pesticides containing inorganic mercury or arylmercury compounds should be retained. However, even these registrations should not be retained if the use poses a water contamination hazard. Consideration has been given this report in the present study.

While it would be ideal to follow the outline of uses employed in Chapter I of this report, this was not done in consideration of the human hazards associated with the use of mercurial pesticides. Therefore, the uses have been categorized under two headings: VII.B.1. Pesticides Containing Alkylmercury Compounds, and VII.B.2. Pesticides Containing Metallic Mercury, Arylmercury or Inorganic Mercury Compounds. The human toxicity of the alkylmercuries is discussed under VII.B.1. without regard to the environmental contamination potentials. The environmental contamination potentials of mercurial pesticides are considered in detail under VII.B.2. before the listing of the specific pesticide uses. Individual uses will be discussed at length where necessary; otherwise reference will be made to the particular hazard, if any, which the use involves.

VII.B.1. *Pesticides Containing Alkylmercury Compounds* — The different members of the homologous series of alkylmercury compounds behave in the same manner and can cause the same type of poisoning. The anion of the compounds has no influence on the biological reaction of mammals but may influence some of the physical characteristics of the salt, such as volatility.

The acute toxicity of the alkylmercury compounds is lower than the acute toxicity of the soluble inorganic mercury compounds and of the arylmercury compounds. However, the alkylmercury compounds are absorbed from the gastrointestinal tract to a much greater extent than are the inorganic or arylmercury compounds.

The greatest physiological distinction between the alkyl and aryl or inorganic mercury compounds is the distribution of mercury within the body after single or repeated administrations. Inorganic mercury compounds disappear rapidly from the blood, and the blood concentrations of mercury remain low even after repeated administrations. The arylmercury compounds disappear rapidly after a single administration, but after repeated administrations, there is a considerable increase in the blood content of mercury. The greatest increase by far is caused by the alkylmercury compounds.

Inorganic compounds of mercury give concentrations of mercury in the kidneys of from 100 to 1,000 times that found in the blood. The arylmercury compounds give kidney concentrations of from 2 to 100 times that found in the blood. However, this concentration increases with time as the result of the conversion of phenylmercury to inorganic mercury in the liver. The concentration of alkylmercury compounds in the kidney is about 1.0 to 1.4 times that in the blood.

The concentration of mercury in the liver after inorganic mercury administration is from 5 to 20 times that found in the blood. The arylmercury compounds give about 2 times that in the blood. The alkyl compounds give a liver concentration of only about 0.2 to 0.4 times that in the blood.

The mercury concentration in the brain after the administration of inorganic mercury salts is about equal to the blood concentration. After the administration of aryl compounds, it is only 1 to 3% of that in the blood. Alkylmercury compounds give a brain concentration of only about 4 to 6% of that found in the blood. However, as the mercury in the blood is much higher after the administration of the alkylmercury compounds, the mercury retained in the brain after the administration of this compound is by far higher than after equivalent amounts of the other compounds of mercury.

The placenta is an effective barrier to mercury derived from inorganic or arylmercury compounds. However, this is not true with alkylmercury compounds. After the administration of these compounds, the mercury concentrations in the fetus may reach higher levels than those found in the maternal tissues. The chromosome-damaging and teratogenic effects of the alkylmercury compounds are greater than those of inorganic or arylmercury compounds.

The alkylmercury compounds are excreted much more slowly than are the aryl or inorganic mercury compounds. This indicates a considerable risk for accumulation of alkylmercury compounds on repeated exposure.

Serious poisonings and fatalities resulting from the manufacture and handling of the alkylmercury compounds have been described in the literature. Hundreds of people have been poisoned from the consumption of wheat treated with these compounds; an entire family was poisoned from the eating of meat from hogs fed alkylmercury-treated grain. The fish which caused the epidemic poisonings in Minamata and Niigata contained this compound as did the seeds which caused the drastic reduction in the bird populations in Sweden. It is the opinion of this Special Group that pesticides containing alkylmercury compounds can not be labeled adequately to protect the safety of the public. The Group recommends that the registrations for pesticides containing alkylmercury compounds be suspended, because of the immininent hazard to human health.

VII.B.2. *Pesticides Containing Metallic Mercury, Arylmercury or Inorganic Mercury* — The pesticides comprising this category are considered on the basis of their potential for environmental contamination and on the basis of the possible effect the particular use may have on human health.

VII.B.2.1. *Pesticidal Mercury and the environment* — Mercury resulting from pesticidal use may contaminate the soil, water, or atmosphere. Because of the volatility of mercury and its natural circulation in the environment, mercury contamination of the soil or atmosphere will eventually result in water and food residues.

Pesticidal mercury may reach the soil from a number of sources: from treated seeds or grain; from fall-out following sprayed applications to agricultural and ornamental plants; from the treatment of lawns and turf; from the wash-off of painted structures; and from the emptying of vats in which bulbs, corms, textiles, fabrics, fibers, logs, or lumber were treated.

Mercury may reach water either directly from one of the above applications, e.g., emptying of vats in which fabrics were treated. Mercury may also reach the aquatic environment bound to soil particles or from the washing of the atmosphere by rain.

Mercury may become firmly bound to the soil. This phenomenon of mercury adsorption is intimately related to the type of soil with which the mercury comes in contact. The nature of the colloidal soil particles, whether they are high in organic content or are of clay or sandy composition, affects adsorption. The solubility of the mercury compound and the pH of the soil also affects soil adsorption. The temperature and the condition of soil moisture also play an important role in adsorption (Mrak, 1969). The affinity of certain soils for mercury is indicated by the failure of mercury applied as orchard sprays (phenylmercuric acetate) over a period of several years to migrate below the surface 2 inches; the soil contained 500 or 1,100 ppb mercury depending on the number of spray applications (Ross and Stewart, 1962).

Even in those instances in which mercury is firmly adsorbed to soil, water contamination may result. Mercury held in the soil may be carried by water with possible subsequent contamination of water courses, water supplies, and groundwater. Runoff after either rainfall or irrigation may physically transport particles to which mercury adheres, or the water may leach the pesticide from the soil particles (Mrak, 1969).

Much has been said about the natural background of mercury in the environment. However, it is difficult, if not impossible, to separate the naturally occurring mercury levels from the levels created by man. The upper limit for the natural release of mercury due to chemical weathering can be estimated by comparison with the corresponding figures for sodium. The sodium leached by weathering is almost completely carried to the sea by rivers, $8 \times 10^7$ tons per year (runoff of rivers, $3.2 \times 10^{13}$ tons per year; noncyclic sodium in river waters, 2.5 ppm). In the weathered rock masses, the ratio of mercury to sodium can be estimated to be the same as the ratio of their lithospheric abundances ($2.8 \times 10^{-6}$), which yields an upper limit of 230 tons per year for leached mercury. The amount of mercury released is probably less than this estimate, because proportionally more mercury than sodium is absorbed on clays, hydroxides, organics, and so forth (Joensuu, 1971).

Another source of mercury is the burning of fossil fuels and ores. In order to estimate the amount of mercury released into the atmosphere by the burning of coal, Joensuu analyzed samples of 36 American coals by means of a mercury vapor detector that had been modified to eliminate organic vapors which interfere in the detection process. The mercury content of the Illinois coal samples that were analyzed contained an average of $180 \times 10^{-9}$ g/g mercury. The author applied a more conservative estimate of 1 ppm to the yearly production of coal and concluded that about 3,000 tons of mercury per year are released to the environment by the burning of coal.

The burning of fossil fuels by man contributes more than 13 times as much mercury to the environment as does the natural weathering process. The use of pesticides contributes over two times as much mercury to the environment as does the natural weathering process. It is obvious that man is contributing a substantial amount to the "natural" background of mercury, and we must eliminate all but the essential dissipative uses of mercury.

### VII.B.2.2. *Coatings*

VII.B.2.2.1. *Paints, Varnishes, and Stains* — This is a highly significant use of mercury. In 1969, 720,000 pounds of metallic mercury were used in paint as follows:

| | |
|---|---|
| Interior latex | 45,000 lb |
| Exterior latex | 351,000 lb |
| Exterior oil | 324,000 lb |

Mercurials are added to interior water-thinned (latex) paints to prevent spoilage during manufacture and in the container during storage. The concentration employed for this use ranges from 0.015 to 0.02% mercury as the metal. Solvent-thinned interior paints do not require the use of mercury for preservation.

Mercurials are used in exterior water-thinned paints both for preservation in the container and as a fungicide to minimize discoloration from mold or mildew growth on the dry paint film. For this use, mercury, as the metal, is used in the range of 0.05 to 0.09%. Solvent-thinned exterior paints may also contain mercury to prevent mold growth on the dry film.

The mercury compounds generally used in paints are:

Phenylmercuric acetate
Phenylmercuric oleate
Diphenyl mercuric dodecenyl succinate
Phenylmercuric propionate
Chlormethoxypropylmercuric acetate

(1) *Interior Paints* — In order to satisfy the labeling requirements under the Federal Hazardous Substances Labeling Act, acute oral and dermal toxicity studies were carried out by Hazleton Laboratories for the National Paint, Varnish, and Lacquer Association. These studies indicated paint could contain up to 0.2% elemental mercury without hazard of acute oral or dermal toxicity or dermal irritation.

A study was conducted by Goldwater and Jacobs (1964) to determine the concentration obtained in a room painted with paint containing mercury and the effects on the inhabitants of the room. It was found that a concentration of 0.17 mg/m$^3$ of mercury vapor was reached in 90 minutes after painting. The total mercury concentration was of the order of 0.20 mg/m$^3$ for about 4 1/2 hours. After 24 hours with no exceptional attempts at ventilation, the concentration of mercury decreased to insignificant levels. Some mercury was absorbed by the inhabitants of the room, as measured by comparative excretion concentrations of mercury in the urine. However, the mercury concentration in the urine of the test subjects was no greater than found in the urine of unexposed "normals." No evidence was found of mercury exposure or absorption in a degree that would constitute a hazard to the painters or to the occupants of the room.

As reported earlier, Hirschman, *et al.* (1963), associated acrodynia in a 5-year-old child to the inhalation of mercury vapors in a freshly painted room. Miller, *et al.* associated neuromyasthenia in 49 employees to the exposure of organic mercury from freshly painted walls.

(2) *Exterior Paints* — In their reply to the Federal Register Notice on Mercury, the National Paint, Varnish and Lacquer Association stated that mercury is lost from painted exterior surfaces. The majority of this is washed from the painted surface and goes into the ground. The statement is made that the mercury (phenylmercury) is firmly bound to the soil and is not removed by dilution with water or saline solution. The Association therefore contends that the mercury thus removed from the painted surfaces does not enter the aquatic eco system.

The thesis that mercury thus bound will not eventually end up in water is untenable. Mrak (1969) stated that because of the tight binding characteristics of pesticide residues to soil particles, the general pollution of water by pesticides occurs through the transport of soil particles to which the residue is attached. Soil residues may, therefore, be a cause for concern; since they may reach man by a number of routes; uptake from soil by consumable crops; leaching into water supplies; and volatilization into the air.

The National Paint, Varnish, and Lacquer Association states that there are no substitutes now available for mercury for the preservation of paint; and without preservatives, latex paints will spoil during manufacture. The Association states that it will require 1 year to develop a suitable substitute for mercury in interior paint and 3 years to develop a substitute for mercury for exterior paint.

Paint manufacturers do recycle wash water and use it in the preparation of other batches of paint, thus the manufacture of paint does not contribute to mercury pollution.

This is a highly significant use of mercury. It is the largest dissipative use of mercury in the United States today.

There are latex paints on the market which contain preservatives other than mercury. Therefore, there seem to be suitable substitutes for mercury in the preservation of paint.

(3) *Ship bottom antifouling paints* — This use constitutes a direct contamination of water with mercury. This contamination may result from the slow leaching of mercury from the painted ship bottom or from dust and chips from the ship bottom when it is scraped and sanded prior to repainting. Mercury may be released in acutely toxic amounts during this sanding operation. Schrager (1964) reported on the occurrence of tubular necrosis in a 2-year-old child ex-

posed to mercury during the sanding of a boat bottom. There are safer and equally effective substitutes available for this use.

VII.B.2.2.2. *Other Coatings — Adhesives, Starches, Glues, Emulsions, etc.* — These uses include glues for labels of cans, wallpaper paste, glues for various fabrics, spackling compounds, joint cements. These are in liquid or dry form which are ultimately to be applied by dispersion in water. Phenylmercuric acetate and phenylmercuric ammonium acetate are used for preservation of the products at levels of 45 to 250 ppm. For mildew control in finished products, phenylmercuric acetate or phenylmercuric ammonium acetate levels range from 3,500 to 15,000 ppm.

RECOMMENDATION:

(a) *Interior paints* — The Committee recommends the cancellation of this use, because of the environmental contamination potential. The Committee believes there is insufficient evidence to consider this use as a human health hazard.

(b) *Exterior paints* — The Committee recommends cancellation of this use, because of environmental contamination.

(c) *Shipbottom antifouling paints* — The Committee recommends cancellation of this use, because of direct contamination of water with mercury, and because of acute toxicity to humans.

(d) The Committee considers the use of mercury in adhesives, starches, glues, emulsions, etc., to be equivalent to paint use and recommends that the registrations be cancelled.

VII.B.2.3. *Fabrics and Textiles* — Mercurial pesticides are used as mildew preventatives in fabrics and textiles.

*Indoor Use* — These fabrics are used as bedding, dust cloths, mops, rugs, shoe linings, etc. As such articles will come into intimate contact with humans.

*Outdoor Use* — These fabrics and textiles are used as awnings, sails, tarpaulins, etc.

RECOMMENDATION:

The Committee recommends that all registrations be cancelled.

VII.B.2.4. *Fibers and cordage* — These uses include the interior components of furniture, mattresses, pillows, etc., air-conditioner filters, and rope and twine.

The use in interior components of furniture, mattresses, pillows, etc., and the use in air-conditioner filters may act to increase the body burden of mercury. These uses present a potential human health hazard.

The uses in rope and twine constitute an environmental hazard.

RECOMMENDATION:

The Committee recommends cancellation of the uses on interior components of furniture, mattresses, pillows, and the use in air-conditioner filters.

The Committee recommends cancellation of the registrations in rope and twine.

VII.B.2.5. *Food, Feed, and Tobacco Crops* — These uses of mercury result in a direct contamination of the environment. Alternatives are available. (See Chapter 1).

RECOMMENDATION:

Cancel the food, feed, and tobacco crop uses of mercury.

VII.B.2.6. *Feed Containers* — These are sacks, seed bins, and containers for treated seeds subject to diversion to food and feed use. This use presents not only an environmental contamination hazard but also a potential human health hazard.

RECOMMENDATION:

Cancel this use of mercury.

VII.B.2.7. *Humans* — These registrations are for Mild Mercurial Ointment (Blue Ointment) as a treatment for pediculosis pubis. This product contains elemental mercury which is absorbed through the intact skin. Fatal accidents have been reported in which the entire body surface was covered with Blue Ointment.

RECOMMENDATION:

Cancel the registrations for Mild Mercurial Ointment as a treatment for pediculosis pubis.

VII.B.2.8. *Ornamental Plants*

1. *Bulbs and Corms* — The mercurial fungicides are used to control root, stem, and bulb rots. The registrations include alkyl, aryl, and inorganic mercury compounds. In Washington and Oregon, bulb dipping vats have capacities up to 10,000 gallons. The drainage of the vats after treatment of the bulbs and corms has been completed poses a significant potential for contamination of the soil and water.

2. *Cuttings* — Only alkylmercury compounds are employed in this use.

3. *Flowering and Foliage Plants* — These uses are directly on the foliage of the plants or on the soil in which they are planted. This usage pattern provides a direct contamination of the environment.

4. *Trees and Shrubs* — This use provides a direct contamination of the environment with mercury.

RECOMMENDATION:

Cancel the registrations for the use of mercurials on ornamental plants.

VII.B.2.9. *Paper* — Mercurials are used for moldproofing paper, paperboard, and wallpaper. This use provides a direct contamination of the environment with mercury.

RECOMMENDATION:

Cancel the registrations for the use of mercurials in paper.

VII.B.2.10. *Plastics* — Mercurials are used as fungistats in the plastic films. The use of plastics thus treated range from garbage bags, shower curtains, to almost any nonfood use of plastics. Garbage bags treated with mercury are often misused for the storage of foods.

RECOMMENDATION:

Cancel the registrations for the use of mercurials in plastics.

VII.B.2.11. *Rubber* — The use of mercurials in rubber is similar to the use in plastics.

RECOMMENDATION:

Cancel the registrations for the use of mercurials in rubber.

VII.B.2.12. *Sanitizers*— This category includes impregnated dust cloths and floor wax. Mercury from this usage pattern will eventually enter the sanitary sewers.

RECOMMENDATION:

Cancel the registrations for the use of mercurial pesticides in sanitizers.

VII.B.2.13. *Seed Treatments* — Petitions for tolerance are pending for some uses of mercurial pesticides as seed treatments. Substitutes are available for all uses except for stinking smut on wheat and striped smut on barley.

RECOMMENDATION:

Cancel all registrations for use as seed treatment except for stinking smut on wheat and stripped smut on barley.

VII.B.2.14. *Tanneries* — Mercurials are employed in the tanning process as fungistats. The liquor from this process is a potential contaminant of the environment.

VII.B.2.15. *Wood* — Mercurial pesticides are used to prevent sap stain in freshly sawed logs and lumber and as a preservative of wood against fungi. These uses are a direct contamination of the environment with mercury.

RECOMMENDATION:

Cancel the use of mercurial pesticides as preservatives for wood against sap stain and fungi.

VII.B.2.16. *Sterilization of Dental and Surgical Instruments* — The solution in which instruments are sterilized is discarded into the sanitary sewage system and contaminates water with mercury.

RECOMMENDATION:

Cancel the uses of mercurial pesticides for the sterilization of dental and surgical instruments.

VII.B.2.17. *Surfaces* — As fungistats on commercial, institutional and household surfaces such as cabinets, floors, walls, ceilings, garbage cans, lockers, masonry, tile, refrigerator and other hard surfaces; blankets, canvas goods, carpets, clothing, cubicle curtains, hampers, laundry bags, leather goods, linens, mattresses, uniforms, upholstery and similar porous surfaces. These uses bring mercury into intimate contact with humans and also provide a contamination of the environment.

RECOMMENDATION:

Cancel the uses of mercurial pesticides on environmental surfaces.

VII.B.2.18. *Miscellaneous*

1. *Seam and Bedding Compounds* — These compounds are used in boat-building and provide a direct contamination of water.

2. *Broomcorn* — Mercurial pesticides are used in the process of dying broomcorn as a fungistatic agent to prevent discoloration.

3. *Cellulose Sponges* — Cellulose sponges are dipped in solutions of phenylmercuric acetate for preservation. Disposal of these solutions after use will provide a direct contamination of the environment.

4. *Milk and Urine Samples* — Mercuric chloride is added to milk and urine samples as a preservative. Disposal of these samples will provide a direct contamination of water.

RECOMMENDATION:

Cancel the registrations of mercurial pesticides for the above uses.

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